Vol. VII JUNE, 1932 No. 5

THE AMERICAN HEART JOURNAL

PUBLISHED BI-MONTHLY
UNDER THE EDITORIAL DIRECTION OF
THE AMERICAN HEART ASSOCIATION

PUBLISHED BY THE C. V. MOSBY COMPANY, 3523-25 PINE BLVD., ST. LOUIS, U. S. A.
Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.
Additional Entry at Fulton, Mo.

The American Heart Journal

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The American Heart Journal

VOL. VII JUNE, 1932 No. 5

Original Communications

APICAL SYSTOLIC MURMURS IN CHILDREN

FOLLOW-UP OBSERVATIONS IN 100 CASES*

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THE question of the importance of apical systolic murmurs is one of the difficult problems confronting the physician. Such murmurs are discovered in most cases first by the school physician who sends the child home with a statement that heart disease is present. The parents, greatly perturbed, consult the pediatrician or the family physician. He examines the child, finds the systolic murmur at the apex with little or no evidence of other cardiac changes, tells the parents the child will outgrow the murmur and thus allays their fears to some extent. If a cardiologist is consulted he has little more to offer, although in his own mind he may be somewhat uncertain of the final outcome. Such uncertainty arises because there has been no accurate study made of the progress of such murmurs over a period of years.

There are certain orthodox rules to which the cardiologist may adhere when determining whether the apical systolic murmurs are of organic nature. If the murmur is well transmitted and associated with hypertrophy and fluoroscopic evidence of mitral disease, it is usually considered organic. Or he may follow the criteria of Mackenzie[1] who states that if we find a systolic murmur in a good functioning heart of normal size and rhythm with the absence of anything that would indicate that the murmur is definitely organic in nature, then we may conclude that the heart is perfectly normal. Granted that we could decide absolutely which murmurs are organic and which are not, we should still be unable to give any definite prognosis because it is known that organic mitral insufficiency per se rarely if ever causes cardiac embarrassment. The patient and the doctor are most interested in knowing what the future will bring; will the murmur disappear; will there be complications in the form of mitral stenosis; how long will the patient be able to continue with activity unrestricted?

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A search of the literature reveals innumerable opinions as to the subsequent course of apical systolic murmurs, but these opinions have not been based on followed cases. Most men are in accord with the statement that systolic murmurs at the apex are not reliable evidence of heart disease. Cabot,[2] in fact, does not believe that pure mitral insufficiency can be recognized during life as a clinical entity. Reid[3] finds systolic murmurs in 20 per cent of the university students classified as normal. Fahr[4] finds that 40 to 70 per cent of all children between the ages of six and fourteen years and 35 per cent of otherwise normal individuals in the second decade have systolic murmurs. He states further that if no diastolic murmur appears during one or two years following the last attack of rheumatic fever, and if the size and shape of the heart have not changed significantly, the murmur is probably of no significance. Many of these murmurs are admittedly of no significance, but a certain number do progress to advanced cardiac conditions. In an effort to solve the problem as to how many will ultimately become significant, and if possible to establish criteria whereby we may be able to judge which murmurs will be of significance, we have undertaken this study of 100 cases followed over a period of years.

For the purposes of this survey the patients studied were limited to young persons with uncomplicated systolic murmurs at the apex, either accompanying the first sound or replacing it. Patients showing any other pathological processes, such as acute febrile diseases, nephritis or congenital heart disease, were excluded.

Examinations of the patients reported were made in the cardiac clinic of Mt. Sinai Hospital by the same group of men. Most frequently the patients studied were sent to the Cardiac Clinic by the pediatric department because of the discovery of a systolic murmur.

In this series a complete history of the preceding infections was obtained in all cases studied. After a complete physical examination in which the condition of the cardiovascular system was stressed, an orthodiagram and an electrocardiogram were made. These were repeated at the time of the last examination wherever possible. There were 49 females and 51 males in the survey. The youngest was 2 years of age and the oldest 21 years of age. Seven of the patients were 5 years of age or under, 85 were between 6 and 15 years of age, and 8 were between 16 and 21 years of age. The average age was 10.15 years. The average number of years the patients were followed was 6, while the greatest number of years followed was 15. The cases chosen for the study all had fairly loud apical systolic murmurs, without other complicating murmurs.

There were 2 deaths (2 per cent) during the observation period, one occurring after 8 years of observation, and another after 7 years. The first of these died of subacute bacterial endocarditis, and the second of

pneumococcus meningitis. Neither of these showed signs of cardiac failure.

Seventeen (17 per cent) of the patients developed distinct clinical evidence of mitral stenosis. The earliest case of mitral stenosis was discovered one year after the finding of the systolic murmur. The average development of mitral stenosis occurred 4.7 years after the discovery of the systolic murmur. The criterion for the diagnosis of mitral stenosis in all instances was a distinct presystolic or diastolic murmur at the apex with or without other accompaniments of the condition. In other words, the diagnosis of mitral stenosis was not made unless we were certain of its presence.

Nine patients (9 per cent) developed aortic insufficiency during the follow-up period. The earliest of these occurred two months after the apical systolic murmur was noted. The average development of aortic insufficiency occurred 3 years after discovery of the systolic murmur at the apex. The diagnosis of aortic insufficiency was made on the finding of a distinct diastolic murmur audible at the aortic area or along the left sternal margin.

Four patients (4 per cent) developed combined lesions of mitral stenosis and aortic insufficiency. The earliest of these appeared 3 years after the systolic murmur was discovered while the average appeared 5.2 years after the systolic murmur was noticed.

In all, 30 patients (30 per cent) developed serious valvular complications in the form of mitral stenosis, aortic insufficiency or both. Of the remainder, 60 patients (60 per cent) showed uncomplicated apical systolic murmurs, and 8 patients (8 per cent) showed complete disappearance of all murmurs at the time of the last examination. The small number of patients (8) showing disappearance of the murmur is contrary to the popular conception that the majority of apical systolic murmurs seen in ambulatory children disappear as they grow older. This may be due in part to the care taken in looking for these murmurs. (This information is summarized in Table I.)

TABLE I

FOLLOW-UP FINDINGS IN 100 CASES OF APICAL SYSTOLIC MURMURS

No murmurs	8	per cent
Uncomplicated systolic murmur	60	
Advanced cardiac disease	30	
Mitral stenosis		17 per cent
Aortic insufficiency		9
Combined		4
Deaths	2	

The relationship of the history of rheumatic fever, chorea and tonsillitis to the progress of the cases was studied. Twenty-six patients (26 per cent) gave a history of rheumatic fever. Of these, 5 developed mitral stenosis, 6 aortic insufficiency, 2 combined aortic insufficiency and

mitral stenosis, 10 continued with the apical systolic murmur, and 3 were found to be normal.

Of the 12 patients who gave a history of chorea, 6 developed mitral stenosis; one was found normal, and the remaining 5 continued with the systolic murmur.

In totaling the patients with a history of rheumatic fever or chorea we have 38 patients, 19 of whom developed serious cardiac complications. Therefore, given a history of chorea or rheumatism plus a systolic murmur at the apex we may anticipate a 50 per cent chance of serious cardiac disease.

Of the 17 patients giving a history of serious attacks of tonsillitis, without other rheumatic manifestations, 2 developed mitral stenosis, 2 developed aortic insufficiency, 12 remained with systolic murmurs, and one was entirely normal. Thus of 17 patients giving a history of serious attacks of tonsillitis, four (or 23.5 per cent) developed serious cardiac complications.

Of the remaining 45 patients (that is, those without history of rheumatic fever, chorea or definite attacks of tonsillitis) 4 developed mitral stenosis, one developed aortic insufficiency, one developed both mitral stenosis and insufficiency, 35 continued with systolic murmurs, and 4 became normal. Thus we have six patients (13.3 per cent) without any history of rheumatic fever, chorea, or tonsillitis who developed serious cardiac complications. (See Table II.)

TABLE II

RELATIONSHIP OF HISTORY TO DEVELOPMENT OF SERIOUS CARDIAC COMPLICATIONS

	PERCENTAGE DEVELOPING SERIOUS CARDIAC COMPLICATIONS
History of rheumatic fever	50
History of chorea	50
History of tonsillitis	23
No history of infection	13

These conclusions are in accordance with the findings of Morse[5] who states that in the cases in which rheumatism seemed to be the cause of the cardiac involvement the results were not so good as in the cases in which there was not a definite rheumatic history.

We have also attempted to ascertain whether the presence of fever during the course of observation could be used as a prognostic guide. Seventy patients were found to have had some elevation of temperature (usually between 99° and 100° F.) on at least 2 successive visits. Of these, twenty-five (36 per cent) developed mitral stenosis or aortic insufficiency or both, forty (57 per cent) remained with apical systolic murmurs (one of these, however, died of subacute bacterial endocar-

ditis), and five (7 per cent) showed complete disappearance of the murmur. Of the 30 patients who did not show any elevation of temperature, 6 patients (20 per cent) developed cardiac complication, 21 patients (70 per cent) remained with apical systolic murmurs, and 3 patients (10 per cent) showed complete disappearance of the murmur. We thus have not found the presence of slight elevation of temperature to be of much assistance to us in determining which of the cases would progress to serious cardiac complications.

Of interest is the fact that of the 7 patients 5 years of age or under only 1 developed mitral stenosis or aortic insufficiency, and this was a girl first seen by us at the age of 3 with an apical systolic murmur. This patient's course was uneventful until she had her first attack of chorea 5 years later at the age of eight, and then about 18 months after this she began to show signs of mitral stenosis. Also, 3 of these patients (45 per cent) showed complete disappearance of the murmurs later on. These findings tend to confirm the experience of many observers that systolic apical murmurs in very young children are of no serious significance.

We have also classified the patients according to whether their condition at the last examination was improved, unchanged, or worse, as compared with the first examination. This classification showed that 16 patients (16 per cent) were improved, 44 patients (44 per cent) were unchanged and 40 patients (40 per cent) were worse as far as their cardiac condition was concerned.

Of the 49 females, four have married and have had from one to four children each. One of these patients showed mitral stenosis at the last examination, two showed only a systolic apical murmur, while the third has no murmurs whatsoever.

Forty-three of the patients showed clinical enlargement of the heart at the time of their first visit. Of these, one died and 15 developed mitral stenosis or aortic insufficiency, while 2 patients showed no murmurs at all at the last examination. In other words 37 per cent of those patients showing clinical evidence of cardiac enlargement developed serious cardiac complications.

We next considered the value of the x-ray picture in the prognosis. In thirty patients the orthodiagram at the first examination showed the transverse diameter of the heart to be greater than half the diameter of the chest, that is, showed definite cardiac enlargement. Of these thirty cases, twelve (40 per cent) developed mitral stenosis or aortic insufficiency, two (6.7 per cent) died, while one (3.3 per cent) showed no murmur at the last examination. This checks closely with the clinical finding of enlargement, 37 per cent of those showing clinical enlargement and 40 per cent of those showing orthodiagraphic enlargement developing further cardiac complications.

At the first examination twenty-three of the patients were reported as having negative orthodiagrams, that is, no enlargement and no change in contour. Of these, only two (9 per cent) developed mitral stenosis. Of the remainder, four (18 per cent) showed no murmurs whatsoever, at the last examination, and three (13 per cent) were classified as unchanged at the final examination. From this we may conclude that a systolic murmur in the presence of a normal fluoroscopic examination has small chance (9 per cent in our series) of developing into a serious cardiac complication. This is in line with Berger's[6] findings of the importance of the orthodiagram in distinguishing functional from nonfunctional murmurs.

Electrocardiograms were taken in 76 patients (76 per cent). The P-R interval was found to be prolonged in only one case. There were eighteen instances of right axis deviation and four instances of left axis deviation, while the remainder of the records were essentially negative. The electrocardiogram was found to be of no value in estimating the prognosis.

By way of illustration we shall briefly outline a few of our cases.

CASE 1.—S. P., female, first seen May 20, 1924, at the age of eighteen years. No history of rheumatic fever, chorea, or tonsillitis. At this time the heart showed moderate enlargement to the left. There was an accentuated first sound at the apex, followed by a blowing, musical murmur. The orthodiagram at this time showed mitral configuration with slight enlargement of the left ventricle. The electrocardiogram showed right axis deviation. In October, 1929, a faint presystolic murmur was first heard, and in January, 1930, a faint diastolic murmur was also audible in the third interspace just to the left of the sternum. At the last examination, September 24, 1931, there were moderate cardiac enlargement to the left, a presystolic rumble at the apex, a tympanitic first sound, and a systolic murmur, also a to-and-fro murmur at the aortic area. The blood pressure was 136/60 mm. The patient was working full time as a teacher. During the entire period there were no rheumatic episodes.

CASE 2.—A. S., female, aged nineteen years, admitted October 7, 1922. She had had chorea four years previously. At the first examination there was a systolic murmur at the apex but no enlargement. There was no x-ray picture taken at this time, but in 1926 the x-ray examination showed mitral configuration with additional slight enlargement to left and right (diameter of chest 24 cm., transverse diameter of heart 13.5 cm.). The electrocardiogram was negative. In 1928 a diastolic rumble first appeared at the apex. The last examination, October 6, 1931, showed typical systolic and presystolic murmurs at the apex. She has had four pregnancies during this period.

CASE 3.—S. B., male, aged nine years, admitted April 13, 1926. At this time he was having choreic manifestations. At the first examination there was a systolic murmur at the apex, but no cardiac enlargement. The orthodiagram showed straightening of the middle left cardiac margin but no bulging of the left auricle in the retrocardiac space. (Diameter of chest 19 cm., transverse diameter of heart 9.5 cm.) The electrocardiogram was normal, except for an inverted P-wave in the third lead. In March, 1930, a presystolic murmur appeared at the apex. At the last examination, October 24, 1931, there were a presystolic thrill at the apex, presystolic and systolic murmurs at the apex, and moderate cardiac enlargement to the left. The orthodiagram at this time showed mitral configuration, with slight encroachment of the

left auricle on the retrocardiac space. Incidentally, this boy feels well and engages in school athletics.

CASE 4.—R. G., female, aged three and one-half years, admitted July 3, 1923. There was no history of rheumatic fever, chorea, or tonsillitis. Examination showed a blowing systolic murmur at the apex, transmitted out to the left axilla, but no cardiac enlargement. The orthodiagram at this time showed a transverse heart with no enlargement. (Diameter of chest 14 cm., and transverse diameter of heart 7 cm.) The course was uneventful and the last examination, November 14, 1931, showed no murmurs and very slight enlargement of the heart to the left. The orthodiagram at this time was essentially normal. (Diameter of chest 19 cm., and transverse diameter of heart 8.5 cm.)

SUMMARY

A follow-up study, covering an average period of six years, was made of 100 children with uncomplicated apical systolic murmurs, with the following results:

1. Of all the patients 30 per cent developed serious complications (mitral stenosis, aortic insufficiency or both).

2. Of those giving a history of rheumatic fever or chorea 50 per cent developed serious cardiac complications.

3. Among those showing clinical enlargement at the first examination 37 per cent developed serious cardiac manifestations.

4. Of those showing enlargement by orthodiagram 40 per cent developed serious cardiac manifestations.

5. Only 9 per cent of those with entirely normal fluoroscopic findings developed further evidences of cardiac disease.

6. Only 8 per cent of the patients showed complete disappearance of the murmur.

7. Only one of the seven patients 5 years of age or under developed serious cardiac complications and this patient had an attack of chorea at 8 years of age, following which she developed mitral stenosis.

8. The electrocardiogram seemed to be of no value in estimating the prognosis.

We wish to thank Drs. H. S. Feil and M. L. Siegel for their assistance in the examination of the patients and preparation of the paper.

REFERENCES

1. Mackenzie, J.: Diseases of the Heart, Oxford University Press, New York City, 1925, p. 361.
2. Cabot, R.: Facts on the Heart, W. B. Saunders Co., 1926, p. 293.
3. Reid, W. D.: Heart Murmurs in the Practice of Medicine, New England J. Med. 204: 597, 1931.
4. Fahr, G.: The Significance of the Systolic Murmur, Neb. State M. J. 15: 458, 1930.
5. Morse, J. L.: Prognosis of Acute Endocarditis in Childhood. An Analysis of 100 Cases, Am. J. Dis. Child. 42: 735, 1931.
6. Berger, S. S.: Significance of Systolic Murmurs, Ohio State M. J. 23: 569, 1927.

ROENTGENOGRAPHIC STUDIES OF THE RIGHT VENTRICLE*

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THE right ventricle is a chamber which is particularly difficult to examine by the usual clinical methods. There are many instances where definite information as to enlargement of this chamber is valuable, if not indispensable. Roentgenography of the right ventricle offers methods of study by which this information can be obtained in a sufficiently large proportion of cases to warrant its use as a routine clinical procedure.

Kirch,[1] in recent anatomical and physiological studies, has shown that each ventricle, the right as well as the left, consists of two physiological units, designated as inflow and outflow portions or tracts. That part of each chamber receiving blood from the auricles, formed by the area between the atrioventricular ostium and the apex, is called its inflow tract. The part of the ventricle concerned in expulsion of blood, lying between the apex and the arterial ostium, is called its outflow tract. Below, we shall attempt to show that parts of the inflow and outflow tracts of the right ventricle can be demonstrated radiographically.

It is to be understood that radiography of these tracts must be limited to those portions of the right ventricle which by proper rotation of the patient can be brought into position, so as to outline the contours of this chamber.

In a normal heart, in the usual postero-anterior position, the only part of the right ventricle visible in the cardiac contour is the pulmonic artery and a small part of the pulmonic conus. These are represented by the so-called second curve in the upper part of the left border. Below lies the curve of the left ventricle, and the junction is especially clear in fluoroscopy, where the outward thrust of the conus in systole is in contrast to the inward contraction of the left ventricle. This second curve, then, represents one part of the outflow tract of the right ventricle. It can be further emphasized by rotating the patient into the right anterior oblique position. This rotation brings out the conus and ventral portions of the right ventricle.

The inflow tract, that portion of the right ventricle lying between the atrioventricular ostium and the apex, is best seen in the left anterior oblique position. In this view the subject should be rotated sufficiently (at least 50°) so that the heart is clear of the spine. The lower part of the right cardiac silhouette and the major portion of the diaphragmatic outline will make up the inflow tract of the right ventricle (Fig. 1).

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In this position the body of the right auricle is rotated posteriorly, and the upper part of the right cardiac silhouette is formed by the right auricular appendix (Koch and Wieck[2]) (Fig. 2).

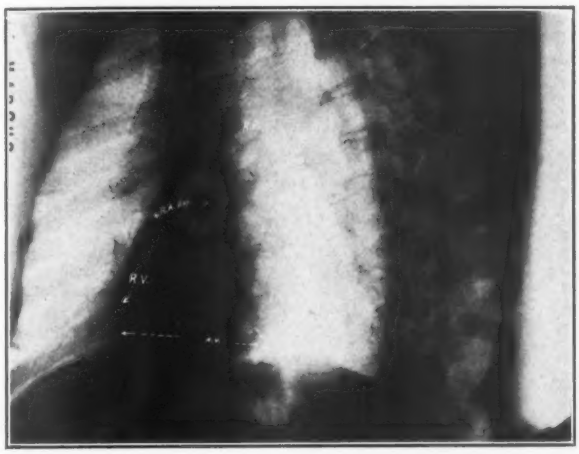

Fig. 1.—Normal heart in left anterior oblique position. In this position a far greater part of the right ventricle can be visualized than in the routine posteroanterior position.

Note the incisura (at arrow) indicating the interventricular groove, forming one terminus of the right ventricle, the other terminus being formed by the lower part of the ventral (outer) border. This part of the right ventricle corresponds approximately to the "inflow tract."

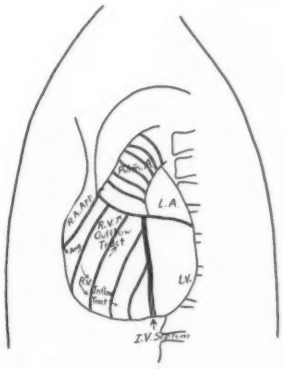

Fig. 2.—Copy of radiograph in left anterior oblique position. The heavy black lines represent metal strips placed around the right ventricle of a cadaver heart in situ. Case of mitral stenosis. Note the extent to which the right ventricle forms the lower and ventral (anterior) borders. The right auricle has been rotated posteriorly and the right auricular appendix forms the upper part of the ventral border. (W. Koch and W. Wieck, *Anatomische Analyse des Roentgenbildschattens des Herzens.*)

On the diaphragmatic surface the differentiation of the parts of the border formed by right and left ventricles can be made only by finding an anatomical landmark which corresponds to the marginal part of the interventricular sulcus.

There have been several attempts to divide the ventricular outline into its right and left components. Bordet's[3] method establishes an apex,

which does not, according to the author's own description, correspond to the terminal portion of the interventricular groove as studied in post-mortem specimens. His established apex is the point lowest and furthest out on the left lower cardiac contour and is found several centimeters from the terminus of the interventricular groove. Only in longitudinal hearts do the two points correspond. In left ventricular enlargement, the points do not coincide, and this apical point is 2 to 3 cm. above and lateral to the interventricular groove.

O'Kane, Andrew and Warren[4] have attempted to reconstruct the course of the interventricular septum in left anterior oblique position, and its termination on the diaphragmatic contour by drawing a perpendicular from a line connecting the upper parts of the two ventricles (the junction of the right ventricle and aorta to the junction of the curves

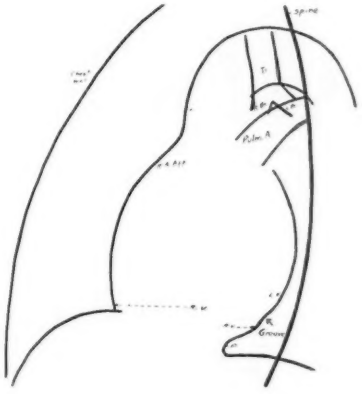

Fig. 3.—Fluoroscopic tracing of a normal heart in left anterior oblique position. Compare with Fig. 2. P indicates one of the points occurring on the diaphragmatic contour which must be differentiated from the groove.

of the left ventricle and left auricle). The point at which this perpendicular transects the diaphragmatic border was considered to be the terminus of the septum.

We have been impressed during routine fluoroscopy in the last three years by the frequency with which an indentation in the left lower contour in the left anterior oblique position has been encountered. This indentation has the appearance of a groove or lip formation and is best seen in deep inspiration and in systole, when this part of the heart is raised from the diaphragm. It was felt that this indentation might mark the interventricular groove at its terminal point. If this contention could be verified, an important landmark would be established, the use of which would reveal the exact participation of the right and left ventricles in forming the diaphragmatic contour. Enlargement of the right ventricle on its lower surface could thus be recognized and the extent of inflow tract involvement could be appreciated (Fig. 3).

METHOD

In order to establish identity of the interventricular groove with the indentation as seen in fluoroscopy, the following steps were taken:

Isolated and unopened human hearts were covered with barium over the lower portions of the interventricular sulcus. The sulcus can be

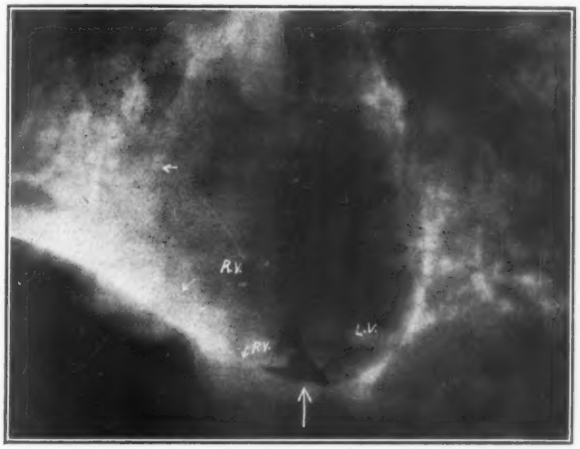

Fig. 4.—Heart-lung-liver dissection in posterior anterior position. Barium mixture in interventricular groove. Note that in this position the direction of the interventricular groove is vertical.

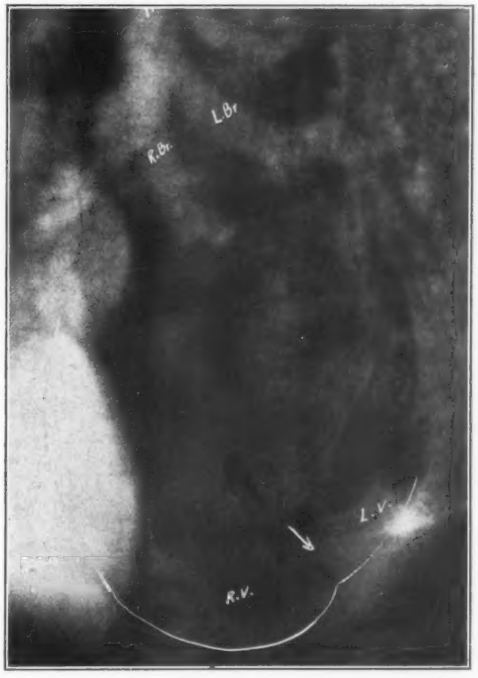

Fig. 5.—Heart-lung-liver preparation in posterior anterior position.

easily identified by the course of the coronary vessels. The specimen was then radiographed in postero-anterior and left anterior oblique positions. In these positions, the terminus of the interventricular groove appeared in the left lower border of the heart. In left anterior oblique, the groove as represented by the barium line corresponded to that seen in fluoroscopy.

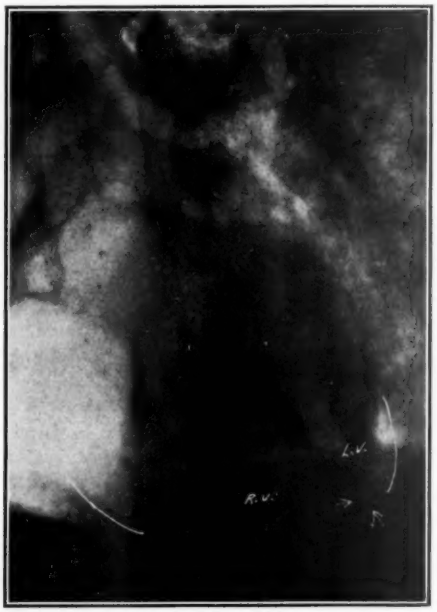

Fig. 6.—Same heart-lung-liver preparation in left anterior oblique position. (Compare with Fig. 5.) The direction of the interventricular sulcus now assumes an oblique course and the base is wide.

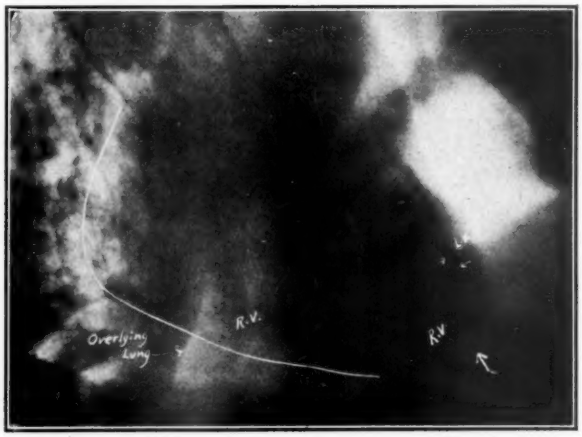

Fig. 7.—Heart-lung-liver preparation. Case of right ventricular enlargement, following chronic pulmonary fibrosis. Radiographed in left anterior oblique position with barium mixture in the interventricular groove. Note marked lower width of heart and position of interventricular groove.

To obtain more accurate data comparable to the positions of the organs in life, dissections of the heart-lung-liver-spleen-stomach were removed *in toto* without disturbing the original relationships, and radiographed in postero-anterior and left anterior oblique positions. The barium line, indicative of the interventricular sulcus, could be clearly recognized. In the postero-anterior position its direction was more or less vertical, in left anterior oblique the direction was oblique with shifting of the lower portions to the left. The position of the groove in left anterior oblique corresponds to the position of the incisura as seen in fluoroscopy (Figs. 4, 5, 6).

In cases of right ventricular enlargement the barium line representing the interventricular sulcus had a lateral oblique course (left anterior

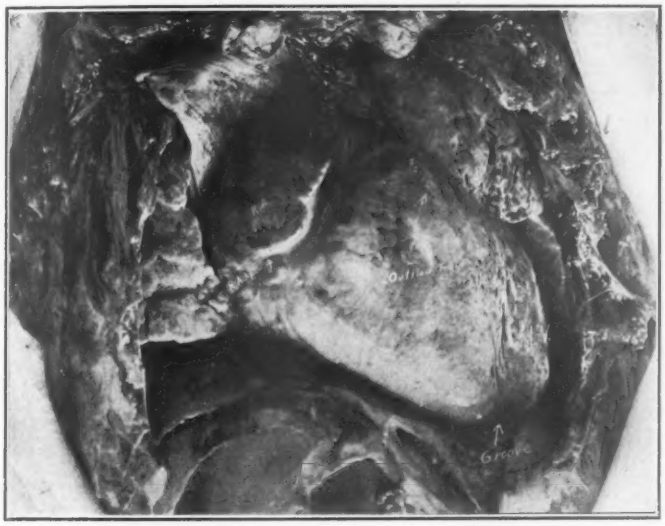

Fig. 8.—Photograph of *Situs Thoracis*. Case of rheumatic valvular disease, mitral stenosis predominating. Illustrates: (a) Marked enlargement of the outflow tract indicated by the prominence of the pulmonic conus. (b) Marked enlargement of the inflow tract indicated by arrows. Note the increased width of the lower border of the heart and the displacement of the interventricular groove.

oblique position) with its terminus on the diaphragm definitely displaced to the left and upward (Fig. 7).

These observations indicate that the incisura as seen in fluoroscopy can be definitely interpreted as being caused by the terminal portion of the interventricular groove. The active systolic elevation of the groove accounts for the difference in appearance of the groove in fluoroscopy from that in postmortem specimens.

It is difficult to demonstrate the incisura in films in the left anterior oblique position. This is due to the fact that the incisura is seen in systole while the radiographic exposure time includes portions of both systolic and diastolic phases. It is likely that with synchronization of exposure with ventricular systole the incisura may be demonstrated in

films in a much greater proportion of cases. Fluoroscopic examination is indispensable and in addition is sufficiently accurate to make such complicated procedures unnecessary.

The incisura caused by the terminus of the interventricular groove as seen in systole must be differentiated from other indentations in this part of the cardiac contour. Such breaks in contour presenting a somewhat angular appearance may be caused by:

(1) The junction of the inferior vena cava with that of the lower outline of the heart. This shadow is usually located to the right in a central position (see Fig. 3).

(2) In a few instances, a shadow similar to the one caused by the inferior vena cava, but further to the left, may be observed. This is situated below the definitely visualized incisura and may be due to the periapical portion of the pericardium.

(3) Another indentation lies between the left ventricle and the left auricle above. This is considerably higher than the incisura, and should cause little difficulty (see Fig. 10).

In general, it may be said that the groove is best visualized in vertical hearts. It is also seen, however, in globular and horizontal hearts in a sufficiently large proportion of cases to make it distinctly worth while to look for it.

In reviewing the literature we found that Pezzi,[5*] observed this indentation, recorded it orthodiagraphically, attributed it to the interventricular groove and attempted to transfer this point to he orthodiagram in the postero-anterior position. No attempts were made by him to observe or utilize this point in reference to right ventricular enlargement.

Koch and Wieck[2] placed metal strips about the individual chambers of the heart in hardened cadavers and then radiographed the thorax in various positions. The interventricular groove was one of these landmarks made visible. This groove corresponds in location and course to that seen in our specimens (see Fig. 2). The groove in neither instance would correspond to the point obtained in the construction of O'Kane, Andrew and Warren.[4] The advantage of our procedure in localizing the interventricular groove is that this is a direct visualization and renders arbitrary constructions unnecessary.

ENLARGEMENT OF THE RIGHT VENTRICLE

Outflow Tract Enlargement.—The first demonstrable enlargement of the right ventricle occurs in the outflow tract in a direction upward and to the left. During the next phase there is increase in mass ventrally and further upward. The right ventricle encroaches on the left ventricle below as well as above. With further encroachment of the right ventricle upon the left, rotation of the heart and aorta takes place. The lateral

*For this reference we are indebted to Dr. H. R. Miller.

parts of the left ventricle are displaced posteriorly bringing the right ventricle forward, upward and to the left (Fig. 9).

The radiographic manifestations of these changes consist essentially of an alteration of the upper and middle parts of the left cardiac border without necessarily any change in the outline of the right cardiac border.

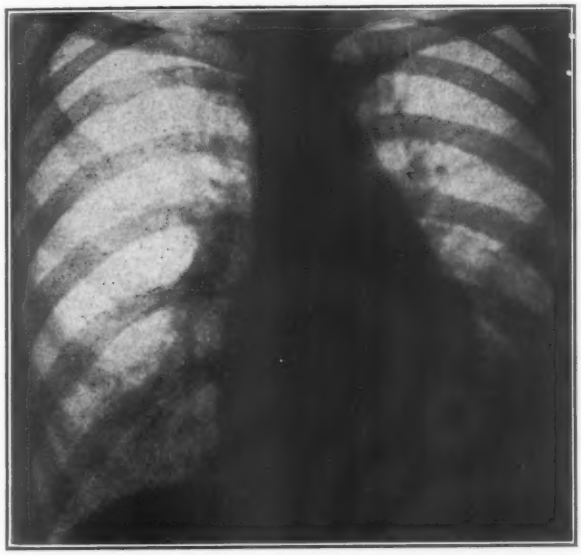

Fig. 9.—Enlargement of the outflow tract. The pulmonic conus is prominent. Note the drop in convexity of the left lower border indicating that the left ventricle is not enlarged in this case. Note also that the heart is not enlarged to the right. Case of mitral stenosis.

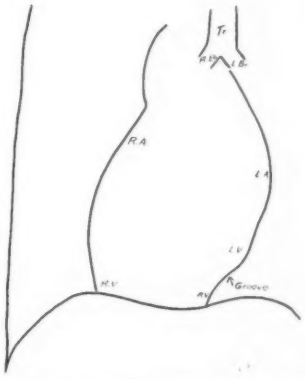

Fig. 10.—Fluoroscopic tracing in left anterior oblique position. Case of mitral stenosis, same as Fig. 9. The interventricular groove is not displaced. The diaphragmatic border is not broadened. Note the indentation between the left auricle and left ventricle.

This absence of enlargement to the right cannot be emphasized too strongly. The varying degrees of this outflow tract enlargement are seen as:

(1) Slight enlargement: increased prominence of the pulmonic artery and conus.

(2) Moderate enlargement: the conus enlargement causes straightening of the normal concavity in the upper part of the left cardiac border (postero-anterior position), prominence of the conus, then actual bulging in this region.

(3) Marked enlargement: still greater enlargement of the outflow tract results in downward prolongation of this bulge or prominence, especially well seen when there is no marked enlargement of the left ventricle (Figs. 9 and 10). (In cases of marked conus enlargement interpretation of the second curve to the left as being due to left auricle has no basis anatomically, except in a few instances when an overlapping of the auricular appendix and the conus may occur.) Enlargement of the

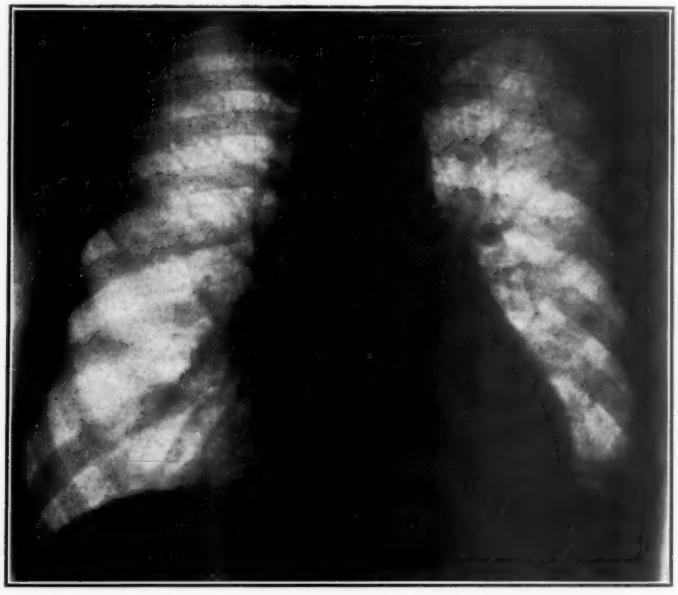

Fig. 11.—Definite enlargement of the outflow tract. The pulmonic conus and pulmonic artery are prominent. There is also some left ventricular enlargement. Heart is not enlarged to the right. The left auricle was not enlarged (autopsy).

outflow tract of the right ventricle, without enlargement of the left auricle or appendix, is sufficient cause to account for all the radiologic changes described above (Fig. 11).

While several of these changes were described in the older radiographic literature, the correlation and interpretation of the above mentioned facts have been definitely established by Assmann[6] and his associates, in whose excellent papers the characteristic radiography and their anatomical bases have been amply correlated. In the American literature, these aspects were recently amplified by Steel.[7]

Inflow Tract Enlargement.—Enlargement of the outflow tract is seen chiefly in the left cardiac border; study of that of the inflow tract requires another method of approach. According to Kirch[1] enlargement

of the inflow tract is first manifested by downward elongation of the chamber from the tricuspid ostium to the apex.* Further enlargement causes additional downward elongation, and broadening of the diaphragmatic surface (Fig. 8). Excessive enlargement of this part of the heart may even displace the right auricle upward and posteriorly to the extent that the right ventricle may actually form a large part of the right lateral border (see Fig. 8), unless there is concomitant excessive enlargement of the right auricle.

To study inflow tract enlargement, we utilize information obtained in the left anterior oblique position. Generally, enlargement of either ventricle will cause an increase in the transverse diameter in this posi-

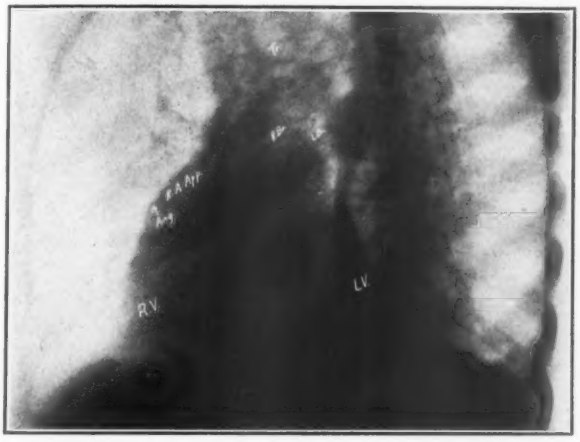

Fig. 12.—Same case as in Fig. 11. Radiographed in left anterior oblique position. Enlargement of the inflow tract indicated by the prominence of the ventral border of the heart below the angulation. The width of the lower border is increased.

tion. When enlargement of the right ventricle predominates, the increase occurs in the ventral (right) portion (Assmann[6]). The part of the right ventricle responsible for this increase is chiefly the inflow tract (Koch and Wieck[2]).

The right anterior border in left anterior oblique position consists of the curves of the right ventricle, right auricle and aorta. The enlarged lower and right lateral parts of the right ventricle (inflow tract) will be projected outward causing prominence in the right lower contour. Enlargement of the right auricle influences the upper part of the right border (Vaquez[8]) (see Fig. 2).

The lower curve of the anterior border representing the right ventricle may be rounded or angular. The angulation, when present, corresponds to the greatest amount of bulging of the right ventricle. It is an important landmark and is definite evidence of inflow tract enlargement (Fig. 12). This angulation may, however, disappear when the enlarge-

*Confirmed by as yet unpublished work of H. Mond, L. Gross and M. A. Kugel (personal communication).

ment of the inflow tract is very marked. It will also disappear when there is enlargement of the right auricle, and the same round contour may result. Certainly it may be said that the portion of the outline below the angulation is right ventricle. Above, it may be either auricle,

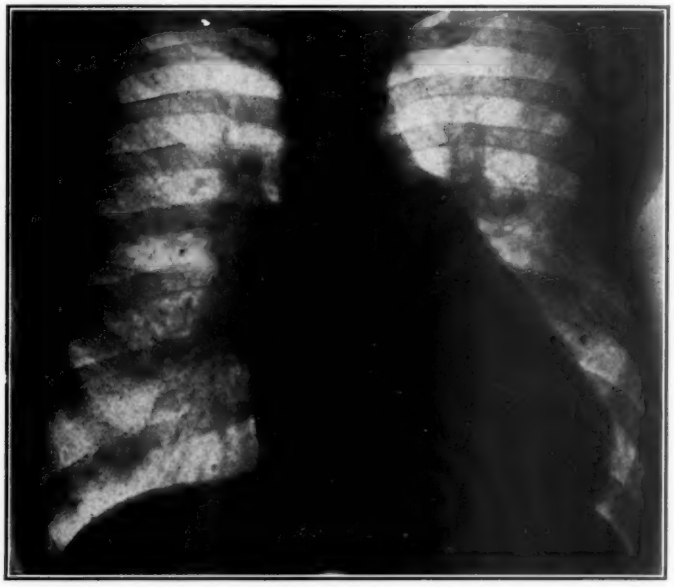

Fig. 13.—Advanced enlargement of the outflow tract. Straightening out and prominence of the left upper cardiac border. No enlargement of the heart to the right.

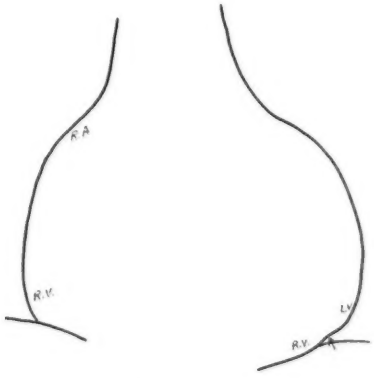

Fig. 14.—Fluoroscopic tracing in left anterior oblique position. Same case as in Fig. 13, marked enlargement of the inflow tract with prominent ventral border, broad lower contour, and displacement of the interventricular groove.

or ventricle and auricle together. It is only in this position (l. ant. oblique) that the right ventricle and right auricle can be differentiated.

The diaphragmatic contour has received little attention, even in the recent literature, chiefly because the differentiation of this outline into

its components is difficult (Assmann[6]). The importance of this much neglected contour has been only recently discussed by Arkussi,[9] who emphasized the significance of right and left ventricular enlargement on the broadening of the base. The localization of the interventricular groove affords differentiation of the diaphragmatic contour into right and left ventricular portions. Enlargement of the diaphragmatic portion of the right ventricle manifests itself (1) in broadening of the base, (2) prominence of the right lower border, (3) and finally, in actual displacement of the groove to the left (Figs. 13 and 14).

There is anatomical evidence of displacement of the septum to the left in right ventricular enlargement (Koch and Wieck[2]). In right ventricular enlargement the septum describes a curve with its convexity to the left. The degree of curvature of the septum in its upper portions does not necessarily correspond to the degree of radiographic displacement of the groove to the left. Inflow tract enlargement may, however, be present without displacement of the marginal portion of the interventricular groove. These observations have been confirmed at postmortem examinations. It follows, therefore, that the displacement of the groove indicates markedly advanced enlargement of the inflow tract of the right ventricle. With the incisuria as a landmark, it was seen that the ratios of portions of the diaphragmatic outline occupied by right ventricle to left ventricle vary from 4 to 1, 5 to 1, or even more, denoting various degrees of right ventricular enlargement. This is contrasted to the 3 to 1 or 2 to 1 ratios observed in the normal left anterior oblique. In right ventricular enlargement the greatest part of the diaphragmatic border as seen in left anterior oblique therefore is contributed by the right ventricle (see Fig. 7).

Enlargement of the left ventricle will tend to displace the septum so that its convexity is to the right. Since the maximal displacement takes place in the upper and not the marginal portions of the septum, it follows that only very marked enlargement of the left ventricle will cause an appreciable displacement of the groove to the right. It seems that enlargement of the inflow tract of the right ventricle displaces the groove more frequently than does enlargement of the left ventricle. This is probably because enlargement of the right ventricle results in rotation of the heart to the left.

In left anterior oblique position the lower ventral border is formed by the right ventricle (the right auricle participating in cases of very excessive enlargement, but not in those of moderate, or even marked enlargement). The diaphragmatic contour up to the incisura is also formed by the right ventricle. Therefore it follows that *an outline representing almost the whole extent of the inflow tract of the right ventricle can be demonstrated radiologically.*

Inasmuch as we have stressed the importance of the groove as a landmark in the differentiation between right and left ventricular contours,

it is necessary to add that there are certain occasions when the incisura cannot be visualized. Such may be the case when the left leaf of the diaphragm is elevated and fixed because of adhesions. Fluid and other shadows also obscure the cardiodiaphragmatic contour. In horizontal hearts with high diaphragm, inspiratory excursions may not be of sufficient depth to reveal the lower segments of the heart. In cases where systolic contractions are superficial and there is no sufficient upward movement with each contraction, the incisura may be suspected but not clearly defined. This is frequently the case when cardiac enlargement is excessive, especially when the left ventricle is so large that the groove is located at or about the center of the diaphragmatic contour of the heart (left anterior oblique position).

Our observations clearly indicate that the segment of the heart resting on the diaphragm in left anterior oblique position consists of the right ventricle. The incisura, when visualized, was found at or near the point where the cardiac contour on the left side rises from the diaphragm. This localization is remarkably constant. While the ventral border may be influenced by excessive enlargement of the right auricle, definite inflow tract enlargement always results in a broadened base extending to the incisura. When the groove is not visualized because of the difficulties mentioned above, we feel that one can assume that the right ventricle reaches to the lower portion of this rising line. This holds true with the exception of those cases where the left ventricle is markedly enlarged on its diaphragmatic surface.

From the above consideration it follows that with the use of the method described, not only is the right ventricular outline defined, but its constituent physiological units are differentiated. To study satisfactorily the right ventricle it is necessary to examine the outflow tract (postero-anterior position), then the inflow tract (left anterior oblique position). Presence of outflow and inflow tract enlargement can so be recorded. It is suggested that this procedure be applied routinely in radiography of the heart, since it gives information not available by any other method.

By applying this method to examination of extensive clinical material we found that enlargement of the outflow tract is easily recognized, even in its early stages, and need not be associated with demonstrable enlargement of the inflow tract. On the other hand, inflow tract enlargement could be definitely shown roentgenologically only when there was considerable enlargement of this portion, and only rarely in the absence of outflow tract enlargement. The cause of the difficulty in recognizing incipient enlargement of the inflow tract lies in the variability of the normal anterior contour in left anterior oblique position. Only considerable deviation from normal will afford positive diagnosis of enlargement.

To evaluate the findings obtained in this study it is necessary to recall the general rule that the object of radiographic examination of the heart is limited at present to recognition of enlargement of individual chambers of the heart. The significance of this enlargement must be reserved for clinical studies to which radiography supplies important data.

SUMMARY

A fluoroscopic method for demonstration of the marginal section of the interventricular groove located on the lower anterior surface of the heart is described, and the application of the method is discussed.

A procedure for systematic radiologic study of the outflow tract and of the inflow tract of the right ventricle is described.

Based upon this study the following criteria for recognition of enlargement of the right ventricle are suggested:

(A) Outflow tract (postero-anterior position).

Prominence of the pulmonic artery and conus on the left upper or on the left upper and middle cardiac border.

(B) Inflow tract (left anterior oblique position).

(1) Prominence of the right lower cardiac border, (2) angulation of the anterior contour, (3) broadening of the diaphragmatic outline, (4) displacement of the interventricular groove to the left and upward.

This study was possible through cooperation of Dr. A. J. Bendick. We are greatly indebted to Drs. D. Perla, V. H. Kugell, and S. Rosen for their valuable assistance in carrying out the postmortem studies.

REFERENCES

1. Kirch, E.: Dilatation und Hypertrophie des Herzens. Klin. Wchnschr. **9**: 769, 1930. Würzb. Abhandl. **22**: 273, 1925.
2. Koch, W., and Wieck, W.: Anatomische Analyse des Roentgenbildschattens des Herzens, p. 25, Jena, 1930, Gustave Fischer.
3. Bordet, E.: Le reperage de la pointe du coeur. Bull. et mém. Soc. de radiol. méd. de France **9**: 69, 1921.
4. O'Kane, G. H., Andrew, F. D., Warren, S. L.: Am. J. Roentgenol. **23**: 373, 1930.
5. Pezzi, C.: Radiol. clin. del cuore. Pp. 39, 48, Cooperativa pamaceutica, Milano, 1928.
6. Assmann, H.: Klinische Roentgendiagnostik der Inneren Erkrankungen, Ed. 4, F. C. W. Vogel, Leipzig, 1929.
7. Steel, D.: Roentgenological and Pathological Findings in Valvular Lesions, Am. J. Roentgenol. **23**: 384, 1930.
8. Vaquez, H.: Maladies du Coeur, pp. 669, 670, Paris, 1921, J. B. Baillière et fils.
9. Arkussi, J. Zur roentg. Character der Funktionsfaehigkeit d. Herzens. Fortschr. a. d. Geb. d. Röntgenstrahlen. **41**: 714, 1930.

FUNCTIONAL LONGITUDINAL BLOCK IN THE HUMAN HEART

A Probable Case With Unusual Arrhythmia*

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INTRODUCTION

THE case with its electrocardiographic record is presented because it represented, we believe, a phenomenon which is in conflict with the present generally accepted opinions regarding the mechanism of the spread of the excitation and contraction waves through the human heart.

A summary of the patient's history is as follows:

CASE REPORT

Miss A. T., a young woman aged twenty-one years, was first observed in the University of California Hospital on September 12, 1924. Her history was characteristic of exophthalmic goiter for three years, with the usual symptoms of weakness, nervousness, loss of weight, tachycardia, a large vascular goiter and ocular changes. She had been under the care of Doctor J. W. James of Sacramento, California, who had treated her for congestive heart failure and thyroid disease by rest, iodine and roentgen ray therapy (thirteen exposures over the thyroid gland and ten over the thymus). She had had alternating periods of tachycardia and bradycardia.

There was a history of involvement of the heart during an attack of scarlet fever at five years of age. There had been several infections diagnosed as influenza, pneumonia and tonsillitis between the ages of sixteen and twenty years.

Physical examination showed the usual manifestations of severe Graves' disease with all the ocular signs associated with the disease including marked exophthalmos. The thyroid gland was of great size and very vascular.

The venous pressure was increased. The liver was slightly enlarged, but there was no edema of the dependent parts. The heart was greatly enlarged to the left. The action was regular, rate rapid, and there were systolic and diastolic murmurs indicative of involvement of both aortic and mitral valves. The systolic blood pressure was 120 and the diastolic was 40 mm. Hg. The basal metabolic rate was 60 per cent above the theoretical normal. The vital capacity was within normal limits.

Teleroentgenograms showed the heart to be enlarged downward and to the left with a straight left border. The apex was rounded. The shadow of the auricles was increased. There was increased density of the shadows over the base of the right lung, and the central markings of both pulmonary fields were exaggerated. There was no evidence of enlarged thymus.

Dental caries was marked and apical abscesses were numerous. Other examinations were unimportant and are therefore omitted here.

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*From the Department of Medicine, University of California Medical School, San Francisco, California.

Read before the meeting of the Association of American Physicians at Atlantic City, May, 1931.

A diagnosis of Graves' disease of marked degree with coincident infectious valvular heart disease with aortic and mitral valvulitis of long standing was made.

The patient remained in the hospital for forty days and was discharged improved. Treatment consisted of rest, high caloric diet, roentgen ray therapy over the thymic region, the insertion of bare tubes of radium emanation (8.0 m.c.h.) into various parts of the thyroid gland and left in situ, iodine in the form of Lugol's solution by mouth, digitalis and alkalies.

The cardiac rate varied from 90 to 120 per minute, and the rhythm was regular until the fifth week when complete heart block suddenly developed, the auricular rate being 130 and the ventricular rate 55 per minute. For three days thereafter the block persisted, and on the third day the auricular rate was 140 and the ventricular rate had increased to 85 per minute. After each second or third auricular complex in the electrocardiogram, the otherwise independent rhythm of the ventricles was disturbed by a response of these chambers, which seemed to take its time from the auricular impulse which preceded it by 0.20 to 0.28 sec. This auriculoventricular block was coincident with overdosage of digitalis and disappeared when the drug was eliminated.

Throughout the period of observation, and before any digitalis was given, the T-waves in Lead III of the electrocardiogram were inverted and there was a moderate degree of right electrical axis deviation.

Upon discharge, the thyroid condition was greatly improved. During the second week of observation the basal metabolic rate had fallen to 44 per cent above the theoretical normal. There was a gain in weight of 6 pounds. With clinical improvement of the Graves' disease it was still more apparent that there was aortic and mitral valvular disease of the heart.

From December, 1924, until February, 1928, the patient pursued a fluctuating course with a gradual trend of improvement in the signs and symptoms of the Graves' disease under oral iodine and roentgen ray therapy. By February, 1927, except for slight dyspnea on moderate exertion and periods of palpitation, she had no symptoms. Signs of aortic and mitral valvulitis were constant. The thyroid gland could not be definitely felt. On one occasion an irregularity of rhythm was noted at examination with apparent coupling of the beats. We were unable to secure an electrocardiogram on this day.

On February 23, 1928, she returned for an electrocardiogram and basal metabolic rate determination. The latter showed 8.8 per cent below the theoretical normal.

The electrocardiogram, taken after a considerable delay which greatly disturbed the patient, was remarkable and is the subject of this report. She was not conscious of having had any attacks of palpitation during that day. Miss Nagle, our technician, observed the irregularity in the movement of the shadow of the fiber after an initial record had been made. Immediately thereafter, Miss Nagle took a second record, the curves of Leads II and III showing the abnormal responses, prior to the termination of the attack. The sequence in taking this record was Lead III, Lead II, and lastly Lead I.

It can be stated with positive assurance that no one else was in the electrocardiographic laboratory except the patient and the technician. Although we have cables to two ward stations, the terminals at the galvanometer are so arranged that these ward stations cannot be connected simultaneously with the laboratory inlets. No one other than the technician had any duties in arranging the electrodes for patients

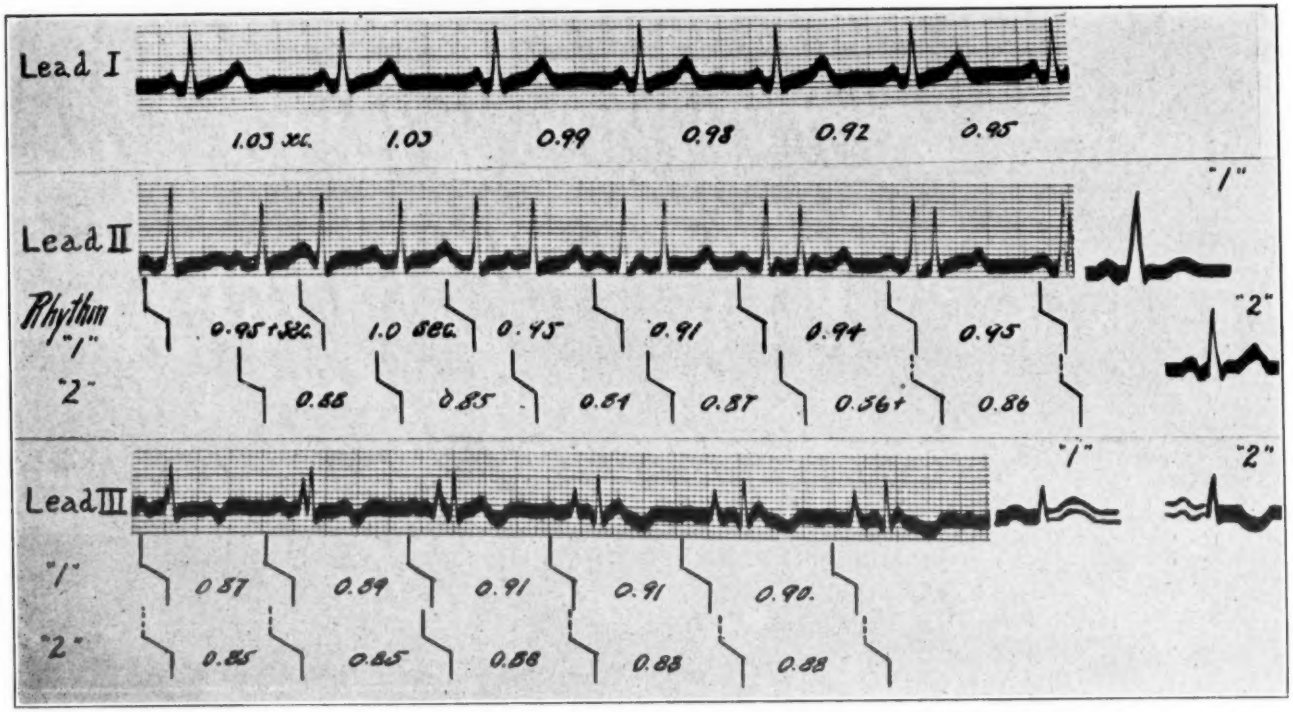

Fig. 1.—Electrocardiogram of Miss A. T. Time interval between beats during the period of arrhythmia indicated in seconds. Freehand tracings of the deflections in the two rhythms indicated by "1" and "2" to the right of Leads II and III. The skeleton portions of these tracings are estimated reconstructions. The vertical lines indicate the positions of the auricular and initial ventricular deflections in each rhythm. No attempt is made to place these lines accurately at the onset of the particular deflections.

at the ward stations or at the central station. The technician could not have been in contact with the body of the patient and have released the plate carrier at the same moment since the couch was several feet removed from the galvanometer. The technician made no direct contact with the galvanometer terminals.

In June, 1928, four months after the unusual curves were obtained all the upper teeth of the patient were removed, and for a month thereafter she had frequent brief attacks of palpitation with great distress and cyanosis. The rate at the apex varied from 30 to 150 per minute as observed by her mother.

We have been unable to observe her in another of these attacks, and interim electrocardiograms have not shown variation in the shape or height of the deflections from the previous records during regular rhythm. The QRS time interval increased from 0.10 to 0.14 sec. in the four years from 1924 to 1928.

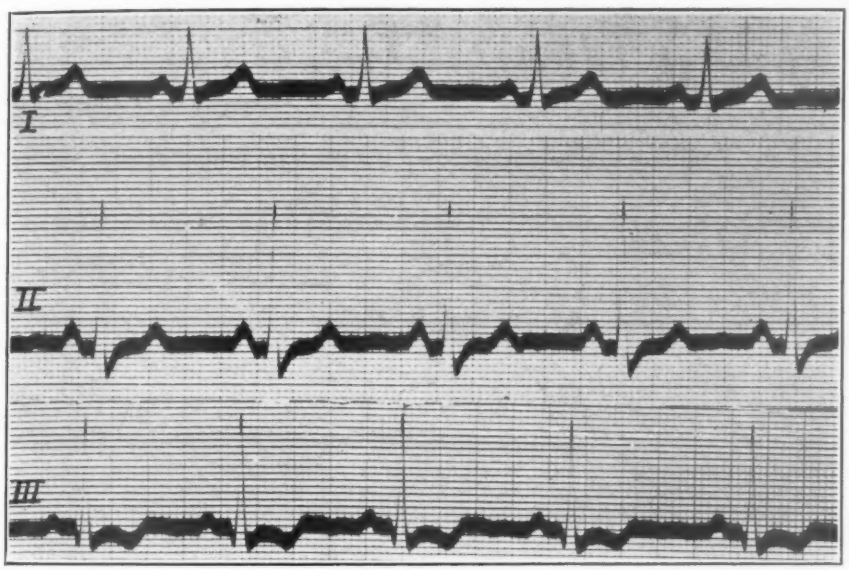

Fig. 2.—The electrocardiogram of Miss A. T. after the period of arrhythmia.

DISCUSSION

Fig. 1 is the electrocardiogram taken during the above described attack with an Einthoven string galvanometer, Cambridge Instrument model. The string calibration was 1 centimeter response to 1 millivolt. The patient was on an isolated circuit with no individual in contact with her or with the electrode leads; and it was impossible for the technician using a standard technic for operating the apparatus to superimpose her own cardiogram on that of the patient, as previously detailed.

It will be seen in an analysis of Leads II and III, taken during the attack, that two independent rhythms, regular but of different rates, are present. Both rhythms have normal P, R, S and T-waves, but the forms of each of these waves differ as will be seen from a reconstructed analysis of them in Fig. 1. What may be called rhythm 1 had a rate

of approximately 80, and what may be called rhythm 2 had a rate of approximately 85 per minute. The P-R intervals of both rhythms are 0.17 sec., as closely as can be measured. It will be observed that there is nearly, although not precisely, the same cyclical variation in both rhythms suggesting the same autonomic nervous system control of both pacemakers.

The patient's normal electrocardiogram, taken on the same day and repeated many times without appreciable alteration in form, is given in Fig. 2, and it will be seen that the P, R, S and T-waves in both Leads II and III are electrical summations of the potentials demonstrated by the individual rhythms during the attack in Leads II and III of the electrocardiogram in Fig. 1. It is believed that this is genuine proof that this remarkable double rhythm was not an artefact.

There is no experimental proof at hand to lead us to draw any certain explanation for this phenomenon if the two auricular and ventricular

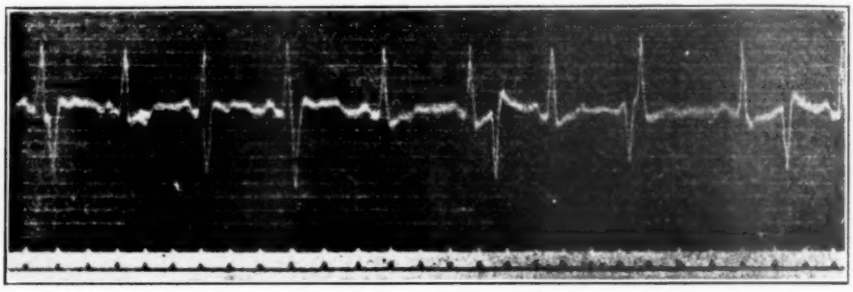

Fig. 3.—Human electrocardiogram from Hoffman which he interpreted as an illustration of longitudinal dissociation.

contractions occur simultaneously and are so completely isolated from each other that there is no influence of one rhythm on the other. If one contraction wave invaded the area of the second wave, the normal refractory quality of the heart muscle, which is presumably present, would prevent a second contraction occurring. On the contrary the second cycle of auricular and ventricular deflections occurs unimpeded during all phases of the cycle of the first rhythm.

An hypothesis may be ventured, namely, that a portion of one or both auricles is responding to a constant pacemaker, independent of the normal pacemaker, with a pathway to one or both ventricles, and, that one or both auricles and ventricles, and the pathway between, are dissociated by all functional contact from the remainder of the heart. [illegible] as if longitudinal sections of the heart were acting independently. Such a phenomenon has been termed longitudinal dissociation but only reported in isolated beats (Hoffman[1]) (Fig. 3*).

*This record has been examined by many cardiologists, and it is uniformly agreed that the possibility of artefact cannot be excluded.

It is not necessary to assume that the dissociation is a true hemisystole phenomenon; nor, if it were such, is there any known proof in man that the auricular or ventricular deflections must be in opposite directions in the independent rhythms?

The unconfirmed work of Kent,[2] published in 1893, illustrated both anatomical and functional pathways between the auricles and the ventricles apart from the normal sino-auricular and auriculoventricular nodes. The work was done on mammalian hearts and has not been adequately checked by repetition. It is conceivable that in the develop-

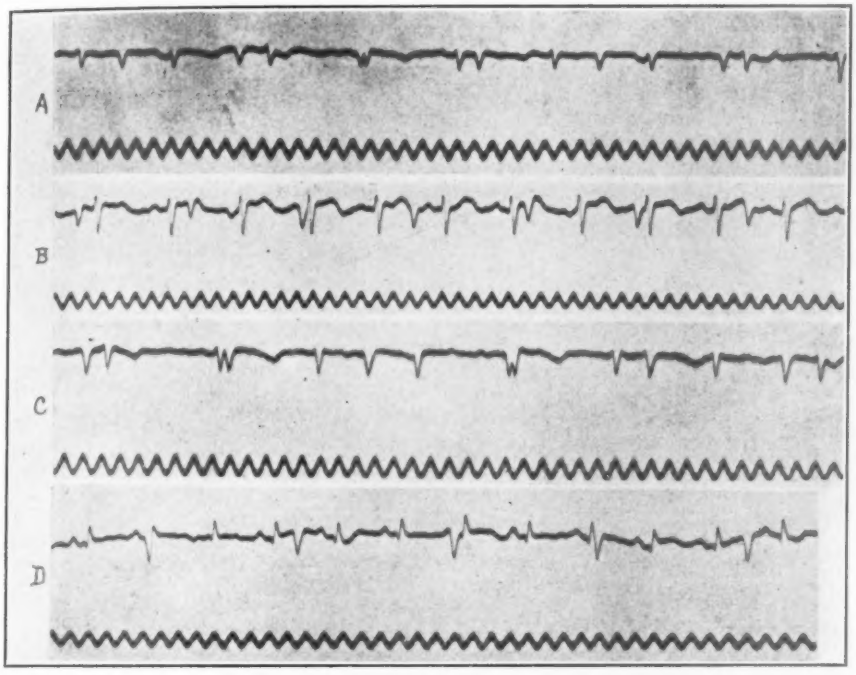

Fig. 4 *A*, *B*, *C*, and *D*.—Four electrocardiograms of newborn infants. (From Burghard and Wunnerlich.)

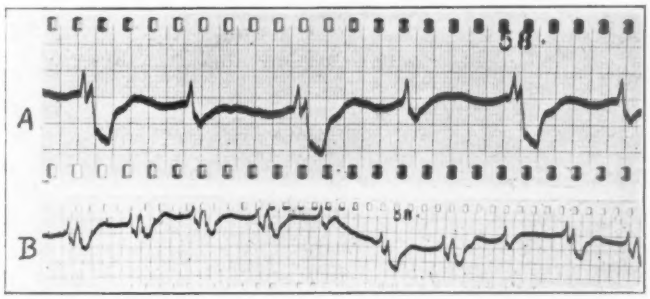

Fig. 5 *A* and *B*.—Electrocardiogram from 90-hour chick embryo. Direct axial leads. Two portions of the same continuous record.

ment of the human heart such a mechanism may be present, through faulty differentiation in the conduction system, after the division of the heart from a two to a three and from a three to a four chambered organ. This faulty differentiation may persist as a functionless anatomical structure in certain hearts with rare periods of reversion of such

a pathway to activity. Only by a fortunate accident could this reversion be recorded. Certain pathological changes may also predispose to this mechanism.

It occurred to us that other evidence of such a pathway could be found in the embryonic heart or in the heart of early infancy. Fig. 4*A*, *B*, *C* and *D* are the electrocardiograms obtained from premature infants by Burghard and Wunnerlich[3] who interpreted the irregularities as recurrent extrasystoles. These records, we believe, illustrate similar dissociation within the ventricles. It is not possible from the curves presented by these authors to determine whether definite auricular waves precede the ventricular deflections.

Fig. 5 illustrates the records that were taken with an amplifying type of galvanometer on one of a series of chick embryos. This particular record was made from a specimen of an approximate age of ninety hours. Here again no auricular waves were recorded, but the heart was grossly observed to contract segmentally along a longitudinal plane. The electrocardiographic record, taken from axial leads, showed apparently the same functional dissociation with evidence that the second portion of the heart was uninfluenced by the refractory period of the contraction waves of the first portion.

CONCLUSION

Whereas it is recognized that no conclusive explanation can be given for the phenomenon observed in this patient, and that the possibility of artefact cannot be completely excluded, we feel that it represents an unusual state of intracardiac dissociation and possibly may be a reversion to an embryonic mechanism.

REFERENCES

1. Hoffman, A.: Die Elektrographie u. s. w., Wiesbaden, 1914, pp. 286-289.
2. Kent. J. Physiol. **14**: 233, 1893.
3. Burghard and Wunnerlich: Ztschr. f. Kinderh. **45**: 56, 1928.

THE STATUS ANGINOSUS INDUCED BY PAROXYSMAL AURICULAR FIBRILLATION AND PAROXYSMAL TACHYCARDIA*

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WILLIAM HEBERDEN[4] in 1768 was the first to give the name "angina pectoris" to the syndrome of paroxysmal substernal oppression on exertion. A great deal has been written about this syndrome since that time, and we have not yet learned the whole story. We have known for years that more factors than one have a part in the production of angina pectoris and only this year Lewis[9] has attempted to separate off one group of cases from the rest, that group consisting of patients with marked hypertension and tachycardia occurring only at the time of the angina pectoris and attributed by him to a kind of vasoconstrictor storm in which the coronary arteries are among the vessels involved. In the present paper we wish to call attention to still another association of angina pectoris, namely that with various types of paroxysmal tachycardia.

It is a fact generally known that sino-auricular tachycardia and a rise in blood pressure frequently occur during an attack of angina pectoris or may bring on an attack. Mackenzie[10] calls particular attention to this, citing a case in which during a test for sensitiveness of the skin of the left breast the heart rate suddenly increased from 90 to 130 with an accompanying severe attack of angina pectoris. Numerous other authors, particularly Lewis[9] during the past year, have written of the increase in blood pressure and also of sino-auricular tachycardia with angina pectoris.

Occasionally angina pectoris and paroxysmal auricular fibrillation or flutter or paroxysmal tachycardia occur in the same patient at different times. Levine[7] found that only one out of 103 cases of angina pectoris showed persistent auricular fibrillation and that one patient showed transient fibrillation; during this same period he saw 423 cases of persistent auricular fibrillation and of this group 200 were observed in elderly persons with "chronic (nonrheumatic) myocarditis." Mackenzie,[10] Lewis,[8] and White[12] have also called attention to the infrequent association of angina pectoris and auricular fibrillation. It is a common clinical finding that when persistent auricular fibrillation sets in angina pectoris usually disappears. However, paroxysmal auricular fibrillation is not so rare in patients with angina pectoris.

Infrequently, paroxysmal auricular fibrillation or paroxysmal tachycardia is found complicating acute coronary occlusion. This fact has

*Presented by title at the Annual Meeting of the Association of American Physicians, Atlantic City, May, 1931.

been noted by various writers; for example, Robinson and Herrmann[11] reported that of four cases of paroxysmal ventricular tachycardia, one had coronary thrombosis (proved at postmortem examination).

Frequently, discomfort occurs with paroxysmal auricular fibrillation, paroxysmal auricular flutter, or paroxysmal tachycardia, but such discomfort is not generally of the nature of angina pectoris. Lewis,[8] in his discussion of the symptoms of paroxysmal tachycardia, included in one group of such cases "anginal symptoms, varying in intensity from slight precordial pain or a sense of compression with skin tenderness to the violent continuous pain radiating in the characteristic fashion over the chest into the neck, into the left arm, or both arms, and into the abdomen." Barnes and Willius[2] reported 19 cases of paroxysmal tachycardia with pain similar in type and location to that seen in angina pectoris but of longer duration, the pain occurring only with the paroxysms of tachycardia. The patients did not have angina pectoris between the paroxysms. Laslitt,[6] among others, has noted pain occurring during paroxysmal auricular fibrillation, but not characteristically anginal.

Finally, *angina pectoris is induced in rare cases as a status anginosus by paroxysmal auricular fibrillation, paroxysmal auricular flutter, or paroxysmal tachycardia in patients who already have shown angina pectoris on effort.* It is the purpose of this report to call attention to this combination which, though rare, is of considerable importance, particularly because of the need of differentiating it from coronary thrombosis.

Three of the four case reports recorded herewith illustrating this condition were obtained from the records of 4,000 cardiac patients seen in our private practice. For the remaining case report we are indebted to Dr. Frank M. Howes of New Bedford, Mass. We have searched the records at the Massachusetts General Hospital without being able to find a clear-cut case of this syndrome. There were several doubtful cases.

CASE REPORTS

CASE 1.—*Angina pectoris and paroxysmal auricular fibrillation.* W. P. B., a married woman of sixty-eight years, was seen on August 3, 1930, by Dr. Howes.

The essential points in her past history were that there had been no illness except colds, and no pregnancies. For the past three or four years she had had pain under the sternum on exertion, with distress radiating down both arms.

On August 3, 1930, while quiet at home, she complained of pain in the chest, substernal in location and radiating down both arms. This pain felt exactly like her angina pectoris of effort but it occurred while she was quiet and persisted for hours. Dr. Howes was summoned and administered morphine subcutaneously. He thought at the moment that he was dealing with acute coronary thrombosis but later events caused him to change his mind.

Physical examination at this time (August 3, 1930) revealed a well-developed, slightly obese woman. Her color was good and the pupils were normal. The teeth were false except for six in the lower jaw in front. A small adenoma of

the thyroid was felt. The heart borders could not be made out. There was a blowing apical systolic murmur replacing the first sound, and a rough systolic murmur was heard in the aortic area also. The rhythm of the heart was absolutely irregular at a rate of 120 beats per minute. The systolic blood pressure was 140 mm. of mercury. There was no edema of the lungs or extremities.

The auricular fibrillation stopped while the patient was being examined and the pain went away at once. The rhythm was then regular at a rate of 68 beats per minute. There were no sequelae even suggesting coronary thrombosis.

The patient was digitalized and then given a ration of one and one-half grains of digitalis five days per week. She has continued to have definite angina pectoris associated with exertion. The blood pressure has varied from 160 to 194 mm. of mercury systolic and from 80 to 88 mm. diastolic. The pulse has remained regular at a rate of 68 to 70 beats per minute, except during paroxysms of fibrillation. She has had three such attacks lasting for one to three hours and each attack has been accompanied by angina pectoris.

CASE 2.—*Angina pectoris and paroxysmal auricular fibrillation.* C. R. S., male, aged sixty-two years at the time of his first attack of paroxysmal auricular fibrillation with angina pectoris in December, 1929, was seen by us in consultation for the first time on January 17, 1928. He had always been well and active, except for occasional attacks of gout and an appendectomy in 1892, until 1908 when he first began to feel on exertion, such as golfing uphill, low substernal distress and pain, radiating upwards and outwards part way to the axillae, more on the left. When the oppression was more severe he would notice, in addition, aching in both wrists, but not in the arms or hands. This pain would last five to ten minutes and would disappear on resting. At that time the pain did not interfere with his work or play, but there was a gradual increase in the frequency of attacks and to some extent an increase in severity of the attacks. During the two years prior to consultation he had been greatly crippled by the angina pectoris and had led a retired, sheltered, and inactive life. The attacks might occur several times in twenty-four hours. As he was very sensitive to nitroglycerine he did not use it much but said that he found aspirin somewhat helpful.

On physical examination he was found to be well developed and nourished. His pupils were equal and active. The lungs were clear. The liver was not felt. There was no edema of the extremities. The maximal apex impulse of the heart was felt under the sixth rib, 9.5 cm. to the left of the midsternal line and 1 cm. beyond the midclavicular line; the left border of dullness corresponded. There was a moderate blowing aortic systolic murmur, heard less well at the apex. The rhythm was regular and the pulse and apex rates were 72 per minute. The blood pressure was 170 mm. mercury systolic and 70 mm. diastolic. The electrocardiogram showed normal rhythm, at a rate of 80, moderate left axis deviation, and rather wide S-waves in Lead II.

He was seen again by us on September 14, 1928, and stated that his angina pectoris had continued more or less the same until about one month prior to this visit when it began to get much worse and he had had daily attacks. He found he could take nitroglycerine grains 1/200 and this dose gave quick relief. Physical examination and electrocardiogram were essentially as before.

He was next seen by us at his club on December 21, 1930, at which time he was in the midst of a paroxysm of auricular fibrillation, the ventricular rate being 120 to 150. He had severe precordial and substernal pain which had at once required 1/8 grain of morphine sulphate subcutaneously, then 1/4 grain more just before we saw him, and finally 1/6 grain in addition one-half hour later. The paroxysm had begun after dinner and was quickly attended by the pain. Nitrites gave no relief. He was taken to the hospital where the palpita-

tion (a relatively slight symptom) and the pain (severe) continued, although numbed by the morphine, until four-thirty the following morning (a total of eight and one-half hours). He slept the remainder of the night. When seen in the morning his pulse was regular at 80; he looked well and was free from pain. An electrocardiogram taken that same day showed normal rhythm, at a rate of 75, with marked left axis deviation.

He admitted at this time (December, 1930) that during the previous year he had had angina pectoris daily, and that there had also occurred, mostly after dinner in the evening, or later at night, spells of auricular fibrillation once or twice a week, attended by persistent pain and lasting a few hours.

He was seen again in his rooms on the afternoon of April 2, 1931. At 8:30 A.M. there had begun his first attack of absolute arrhythmia (with great pain) since the previous November. He had been given morphine sulphate 1/4 grain subcutaneously at noon and had gotten relief from this in two hours. At 3:15 P.M. the heart was absolutely irregular at a rate of 130. At 8:30 P.M. he felt much better, was without pain, and the pulse was regular at 66.

He quickly recovered from this attack, returned to his usual state of health, but died suddenly on June 16, 1931.

CASE 3.—*Angina pectoris and paroxysmal auricular fibrillation.* E. de C., female, aged seventy-five years, was first seen by us as a private patient on December 29, 1930. She said that she had been always well and active but nervously sensitive. For the past year she had noticed substernal oppression on exertion, especially on hurrying or on walking uphill, which oppression had been quickly relieved by rest or nitroglycerine which she had used a few times. She had had some dyspnea on exertion for the year prior to consultation.

About eight or nine months prior to this visit she had had a spell of rapid, irregular palpitation with severe anterior chest pain lasting several hours. She had a second similar spell two or three months after the first.

On December 19, 1930, during dinner and after an unusually active day, she was seized by severe pain under the right scapula radiating down the right arm and lasting for one and one-half hours unchanged, and less severely for several hours after that. She did not notice any palpitation at first but when Dr. James Faulkner saw her an hour after the onset of the attack, he found a rapid irregular heart rate (auricular fibrillation). The blood pressure at this time was 135 mm. mercury systolic and 90 mm. diastolic. The lungs showed moist râles at both bases. There was little or no cyanosis. Pantopon, gr. 1/3, and digitalis, 0.7 gram, were given and the next day the heart rate had dropped to 108 but was still absolutely irregular. Normal rhythm returned spontaneously about thirty-six hours after the onset of the attack. There was no fever after this attack or other evidence of coronary thrombosis.

On physical examination in our office on December 29, 1930, she appeared but slightly ill. Her color was fair and she was breathing normally. There was no engorgement of the cervical veins. Her heart was enlarged, the sounds were of good quality, and there were loud apical and moderate basal systolic murmurs. The rhythm was normal and the rate was 84 per minute. The blood pressure was 200 mm. of mercury systolic and 90 mm. diastolic. The electrocardiogram showed auricular premature beats at a heart rate of 105, and bundle-branch block.

It was reported by letter from Florida on April 1, 1931, that she had done very well until two to three weeks prior to that date when jaundice began. As this did not clear up she was operated on and two gallstones were removed. Her condition was more or less critical for a few weeks but she recovered and returned north.

On May 14, 1931, she was found dead in bed in the morning.

CASE 4.—*Angina pectoris and paroxysmal tachycardia.* W. E. C., male, aged sixty-six years, was seen in consultation by us on July 24, 1930. His past history was irrelevant. His present illness started a few years before his visit to us when he began to notice slight high substernal oppression on considerable exertion such as walking fast up a hill. This would last only a few minutes and there was no radiation. Early in May, 1930, he first began to have spells of weakness. The first two came on after breakfast about two weeks apart and lasted ten to fifteen minutes, passing off with rest.

On May 25, 1930, while at work in his drug store he was suddenly seized by a cold sweat and weakness. He had to sit down and in a few minutes he experienced substernal pain radiating to the left shoulder and down the left arm to the wrist. He was taken home and given morphine sulphate subcutaneously. The pain lasted an hour or more. He remained in bed one and one-half days; there was no fever. He then resumed work but that night he had a very mild brief attack of precordial burning. He then felt all right for over a month but he spent three weeks in bed.

On July 19, 1930, after having been out riding in the afternoon he was suddenly seized, while brushing his teeth, by a spell of racing of his heart followed in five minutes by severe substernal and left arm pain requiring three-eighths of a grain of morphine sulphate subcutaneously. Physical examination that night by Dr. John Sproull revealed a well-developed and nourished man lying flat in bed without cyanosis. He was in a cold sweat. There were rapid pulsations of the veins of the neck. The heart rate on repeated counts was 196 per minute, and the sounds were tic tac in character, but the rhythm was regular. The blood pressure was 120 mm. mercury systolic and 100 mm. diastolic. The rate continued the same for four hours after the administration of morphine but the pain gradually went away in an hour or so under the influence of the drug. The next day he felt all right and continued to feel well although he rested in bed until the day of his office visit to us (July 24, 1930).

On this date his physical examination revealed frequent premature beats, a pulse rate of 80, no evidence of congestive failure, good heart sounds, and heart about normal in size. There were no murmurs. The blood pressure was 120 mm. mercury systolic and 80 mm. diastolic. Fluoroscopic examination showed a normal heart with considerable tortuosity of the aorta. The electrocardiogram showed ventricular premature beats at a rate of 95 with intraventricular block.

A diagnosis of coronary disease with aortic sclerosis, paroxysmal tachycardia, angina pectoris, and intraventricular block was made.

SUMMARY OF CASE REPORTS

Case 1: Definite attacks of angina pectoris on effort, free of tachycardia, during four years prior to consultation. Observed during an attack of status anginosus brought about by paroxysmal auricular fibrillation and disappearing immediately upon cessation of the paroxysm of auricular fibrillation.

Case 2: Definite angina pectoris on effort for twenty-three years. During the last eighteen months of his life he had several attacks of status anginosus brought on by paroxysmal auricular fibrillation; between the attacks of status anginosus he had the usual attacks of angina pectoris on effort.

Case 3: Angina pectoris on effort for about one and one-half years before death. During the last fifteen months of her life she had

three attacks of status anginosus brought on by paroxysmal auricular fibrillation.

Case 4: History of angina pectoris on effort for several years. During the month prior to consultation he had two attacks of status anginosus brought on by paroxysmal tachycardia.

DISCUSSION

Angina pectoris induced as a status anginosus by paroxysmal auricular fibrillation or paroxysmal tachycardia, although rare, should be recognized and differentiated from other conditions, in particular, coronary thrombosis. The points in favor of the diagnosis are as follows: a history of previous angina pectoris, of previous paroxysmal tachycardia or paroxysmal auricular fibrillation, and of their association; the finding of a very rapid heart rate on physical examination at the time of the pain; the demonstration of auricular fibrillation, auricular flutter, or paroxysmal tachycardia by electrocardiogram in patients during the attack of substernal oppression; and finally, the absence of any evidence of coronary thrombosis after the subsidence of the paroxysm of rapid heart action. The course of the illness settles the diagnosis, but at the onset one must in some cases at least remain in doubt. Nitroglycerine is ineffective and morphine subcutaneously is necessary in either case. Quinidine sulphate may shorten the duration of the abnormal rhythm.

Barcroft, Bock, and Roughton[1] made detailed observations on the circulation and respiration in a case of paroxysmal tachycardia. They found that during attacks the systolic blood pressure fell from 120 mm. of mercury to 100, whereas the diastolic rose from 68 to 80 mm.; the minute volume sank from 5 — 6.1 liters to 2.8 — 2.1 liters per minute; ischemia was noted particularly in the skin as shown by analysis of blood from the basilic vein; the systolic output dropped from 77.5 c.c. to 12.9 c.c. They found no reduction in the oxygen saturation of the arterial blood, but rather a rise.

Carter and Stewart[3] studied a similar case and it is interesting to note that during the paroxysmal tachycardia they found a marked decrease in the arterial oxygen saturation without demonstable pulmonary congestion to account for it. They also noted a very low oxygen saturation of the venous blood, largely due to stagnant anoxemia, the result of slowing of the circulation.

When a paroxysm of tachycardia starts, a vicious circle is soon set up, because, the heart rate being increased, there is a greater demand for blood to supply the overworking cardiac muscle; however, the faster the rate, the less the minute volume and systolic output, and hence the greater the decrease in blood supply to the myocardium. Thus it seems quite reasonable, if we accept the theory that myocardial ischemia is a cause for angina pectoris, to account in this way for the induction of the status anginosus by a paroxysm of tachycardia or of auricular fibril-

lation, especially in a myocardium whose coronary circulation is evidently already defective as indicated by the clinical syndrome of angina pectoris on effort.

The ultimate prognosis is apparently as grave in the patient with angina pectoris induced by paroxysmal auricular fibrillation or tachycardia as in the patient with coronary thrombosis, for if there is so much coronary narrowing that an increased heart rate alone (without effort) can induce the pain, life is not apt to be long. Two of the four patients we have reported here died suddenly within two years of the time of onset of their paroxysms of angina pectoris induced by spells of abnormal rapid heart action.

SUMMARY

We have reported here four unusual but important cases to illustrate the fact that a status anginosus may occur without coronary thrombosis.

A great increase in heart rate due to paroxysmal auricular fibrillation or paroxysmal tachycardia (with accompanying drop in systolic blood pressure or pulse pressure) was evidently responsible for the induction of the angina pectoris that was at other times a characteristic result of effort in all of these four cases. Two of the patients were men, aged sixty-two and sixty-six years, and two were women, aged sixty-eight and seventy-five years. One of the men (the first) and one of the women (the second) died suddenly eighteen months and fifteen months, respectively, after the first attack of angina pectoris induced by the abnormal heart rhythm. The other two patients were alive one year after their first attacks of this nature.

REFERENCES

1. Barcroft, J., Bock, A. V., and Roughton, F. J.: Observations on the Circulation and Respiration in a Case of Paroxysmal Tachycardia, Heart **9**: 7, 1921.
2. Barnes, A. R., and Willius, F. A.: Cardiac Pain in Paroxysmal Tachycardia, Am. Heart J. **2**: 490, 1927.
3. Carter, E. P., and Stewart, H. J.: Studies of the Blood Gases in a Case of Paroxysmal Tachycardia, Arch. Int. Med. **31**: 390, 1923.
4. Heberden: Pectoris Dolor. Chapter in Commentaries on the History and Cure of Diseases (translated by William Heberden, Jr.), London, 1802. (The original mention of angina pectoris was made by Heberden in a lecture before the Royal College of Physicians in London in July, 1768, and published in their Medical Transactions in 1786, II, 59, under the title "Some Account of a Disorder of the Breast.")
5. Hirschfelder, A. D.: Diseases of the Heart and Aorta, Lippincott, 1910.
6. Laslitt, E. E.: Pain in Paroxysmal Auricular Fibrillation, Brit. M. J. **1**: 703, 1921.
7. Levine, S. A.: Angina Pectoris: Some Clinical Considerations, J. A. M. A. **79**: 928, 1922.
8. Lewis, T.: Clinical Disorders of the Heart Beat, Shaw and Sons, London, 1920.
9. Lewis, T.: Angina Pectoris Associated With High Blood Pressure and Its Relief by Amyl Nitrite; With a Note on Nothnagel's Syndrome, Heart **15**: 305, 1931.
10. Mackenzie, J.: Diseases of the Heart. Oxford University Press, London, 1913.
11. Robinson, G. C., and Herrmann, G. R.: Paroxysmal Tachycardia of Ventricular Origin, and Its Relation to Coronary Thrombosis, Trans. Ass. Am. Phys. **35**: 155, 1920.
12. White, P. D.: Heart Disease, New York, 1931, Macmillan Company.

TREATMENT OF SPASMODIC VASCULAR DISEASE OF THE EXTREMITIES OF THE RAYNAUD TYPE*

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IN the course of investigations on thromboangiitis obliterans, arteriosclerosis, and related diseases, there have come to our attention a number of cases of peripheral vascular disease which do not conform with the well-known types. These cases seem to resemble mild or borderline forms of Raynaud's disease, presenting such symptoms as acrocyanosis, acroasphyxia, numbness, pain or burning of the fingers or toes. The symptomatology, or rather the emphasis of these symptoms, varied considerably among the cases, but they all had one feature in common, a definite relationship between the onset of symptoms and exposure to cold.

Although none of the four cases described below was of the severity originally noted by Raynaud[1] as characteristic for this disease, they represent at least that variety (described by Lewis) characterized by hypersensitiveness to cold resulting in arterial spasm. They show no permanent, irreversible changes such as gangrene or spontaneous amputation, which probably indicates that spasm formed the essential basis of their symptomatology.

These cases have all been treated by a high calcium regime, and they have all improved. Full histories in these case reports are not here given, since the patients presented no abnormalities other than those noted below.

CASE REPORTS

CASE 1. Mrs. F. H., thirty-two years old, complained for twelve years of coldness and pallor of the fingers of both hands on exposure to cold. For two years, since a thyroidectomy, her condition had been growing steadily worse. Before the beginning of treatment she found that any exposure to cold (going out of doors in cool or cold weather, even with heavy gloves on) resulted in a complete blanching of her fingers, from the tips to the palm, with a numbness and discomfort subjectively, and an extreme coldness of the fingers objectively. After withdrawal from the cold, this stage was followed by a hyperemic red (not cyanotic) stage, which was not painful. Between attacks the appearance of the fingers was normal. Both radial pulses were normal.

After a high calcium regime given by mouth the condition improved, so that the patient never had more than one very mild attack in any single day, no matter how often she was exposed to cold. This mild attack would consist in a blanching of the distal phalanx of one finger only, instead of all the fingers of both hands, as formerly. On intravenous calcium therapy the mild attacks occurred rarely, and there were no severe ones. The appearance of her fingers remained normal when unexposed to cold.

CASE 2. Mrs. M. P., fifty years old, was troubled for two months with attacks of marked burning and blueness of the hands on exposure to cold air. At the onset she had an attack whenever she gripped anything with her hands; later she

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found herself unable to place her hands in cold water without a troublesome sensation of burning, and shortly before beginning treatment she had blueness and burning of her hands on exposure to the outside air.

After one week on the regime she had no more blueness of the fingers, and the burning was markedly diminished. She has had no recurrence now for more than one year, and she has been on medication constantly during that period.

CASE 3. Mr. T. P., twenty-five years old, had been suffering for seven years with dull aching pains in the feet and hands in cold weather. The onset was gradual. There was no history of freezing or other trauma. The condition had been growing steadily worse, so that even moderately cool weather induced the pain. There were no swellings or color changes, but there was markedly local sweating in both hands and feet. The pain was relieved by soaking the painful limbs in hot water.

Treatment was begun in September, 1930, while the weather was still mild and there was no pain. Subsequently, although the excessive sweating has remained unchanged, the patient has been without pain even in very cold weather except for one day when he had pain in his feet while standing outside in the cold during the entire day.

CASE 4. Mr. C. L., thirty-two years old, complained of pain and redness of his hands and feet in cold weather, together with marked itching and sweating. There was no history of trauma.

He improved on dosage smaller than that which we now use, as our present regime had not yet been established. In the course of a month (in February) he reported that his feet were warm, his hands less red, and that the troublesome itching had stopped. When he discontinued treatment for a month, he had a recurrence of symptoms, which disappeared on the resumption of the high calcium schedule.

THERAPY

The therapy consists of a high calcium regime which, in order to be adequate, must take into account the various factors concerned with absorption, such as differences among individuals in the absorptive power for calcium, the addition of vitamins, the time of calcium administration, etc. It is our intention to give in a subsequent communication a full consideration of this question; accordingly we shall here confine ourselves to presenting the following schedule of our procedure in these cases.

For two weeks: A daily diet of milk, 1 quart; viosterol, 30 drops; tomato juice, 16 oz.; orange juice, 8 oz.; and lactose, ½ oz.

The viosterol may be taken in three doses of 10 drops each, or in two doses of 15 drops each.

The tomato juice is given for its high vitamin content, primarily for vitamin B, which favorably affects intestinal tonicity.[2] If tomato juice is not well tolerated, other substances rich in vitamin B may be substituted.

The next two weeks: If results are not satisfactory, calcium salts are substituted for the milk. Either calcium lactate or calcium gluconate may be used.

Dosage of calcium lactate: 80 grains daily in two doses of 40 grains each, 40 grains one hour before breakfast and 40 grains fours hours after supper. If the second dose interferes with bedtime, it may be taken four hours after luncheon, and supper should then not be eaten within less than one hour after taking the dose.

Dosage of calcium gluconate: 150 to 180 grains daily, as either a powder or a tablet, plain or effervescent, the time of administration being the same as for the lactate.

The time of administration of the calcium salts is very important, and only small amounts of water should be taken with the tablets. It has been shown that calcium is absorbed best in the interdigestive period[3] and that when calcium is taken "three times a day after meals," as it is so frequently prescribed, a minimum absorption results and the therapy usually fails.

The next week: If there has been no improvement, calcium gluconate administered intramuscularly is added to the treatment. The dosage is 1 ampule (10 c.c. of a 10 per cent solution) daily, with or without parathormone, 20 units (1.0 c.c.).

The next week: If this has not been satisfactory, calcium gluconate or calcium chloride is given intravenously. The dosage is 1 ampule (10 c.c. of a 10 per cent solution) daily.

LITERATURE

The recent literature concerning Raynaud's disease makes little definite mention of calcium as a therapeutic agent, notwithstanding repeated references to it in the older literature.[4] Osler, for example, in his textbook,[5] lists calcium lactate, gr. xv three or four times daily, as being very effectual in some cases. Calcium is included briefly by Mumford[6] and by Claude and Tinel[7] in describing treatment in their cases. Neither Poulton[8] in 1926, nor Deschamps[9] in 1929, in reviews of the literature on Raynaud's disease with extensive bibliography, considers calcium. Barath[10] mentions calcium briefly, saying that it has been used by many with little success in angiospastic conditions. Margolin[11] in 1926, described Raynaud's disease occurring in a case of tetany, with the cure of both diseases by the administration of calcium.

In related conditions, such as erythema pernio and acrocyanosis, calcium has been used for many years.[12]

THEORETICAL

The explanation for the results obtained in our cases of vasomotor spasm by the use of a high intake of calcium is not entirely clear. Possibly the action of calcium upon this type of vascular spasm caused by cold is analogous or even related to its action in certain so-called allergic conditions characterized by spasm, e. g., bronchial asthma, in which favorable results are often obtained. The analogy becomes even more striking from a consideration of the observations of Thomas Lewis,[13] in cases of Raynaud's disease, that apparently there exists in these subjects a true specific idiosynerasy or hypersensitiveness to cold which manifests itself through the spasmodic arrest of circulation in the affected parts, independently of the vasomotor nerves.

On the evidence presented by Lewis it seems warranted to question the old idea that the disease is one of the nervous system, and particularly related to the sympathetic nervous system. The newer conception is well summarized by Blackader,[14] who says: "The abnormal element in the syndrome would appear to be a local direct reaction to a lowered temperature, due to a peculiar hypersensibility of the vessel wall, and not the result of a reflex through the vasomotor nerve. . . . The pathological element in the vascular spasm is not of central nervous origin as it has generally been thought to be, and there would appear

to be no foundation for relating this vascular phenomenon with diseases of the nervous system in other portions of the body. Recent research points to the possibility of its being due to some deficiency of calcium in the blood."

In considering "calcium in the blood" it should be understood that the total calcium of the blood serum may be a poor indicator of the calcium activity in the body unless it is very high or very low. For example, in long continued hyperparathyroidism, both clinical and experimental, the serum calcium may drop from its initial elevation into the normal range, while the abnormal drain of the body's calcium stores persists as before.[15] In hyperthyroidism, where there is a large negative calcium balance over long periods of time,[16] the serum calcium seldom gives indication of the calcium loss. The reverse of this situation may be exemplified in those occasional cases of tetany with normal serum calcium level, in which, despite the "normal" blood figure, the symptoms may be ascribed to physiological lack of calcium.[17] Since calcium may be found in the blood in three forms (nondiffusible, diffusible ionic, and diffusible nonionic), it is evidently possible for a total concentration to be within normal limits, while an imbalance among these three forms underlies a physiological disturbance. Our methods of precision are not yet adequate in measuring these forms of calcium.

Percival and Stewart[18] investigated the blood calcium in twelve cases of chronic erythema of the legs resembling erythema pernio or mild forms of Raynaud's disease, and found values ranging from 9.2 mg. to 11.8 mg. per 100 c.c. of serum. In two cases they found 73 per cent and 80 per cent diffusible calcium (by collodion filtration). They administered parathyroid by mouth with no improvement, although the serum calcium rose from 9.2 to 10.6, and from 10.0 to 10.3 respectively (obviously not a significant rise). They conclude that hypocalcemia is not an etiological factor in the disease, nor is calcium effective as a therapeutic agent. They made similar studies in other skin diseases,[19] such as Bazin's disease, chronic leg ulcers, psoriasis, and erythema pernio, and came to like conclusions. Hallam[20] accepts their conclusions, saying: "The present state of our knowledge of calcium metabolism is admittedly deficient; but according to the investigations of Percival and Stewart already cited, there does not seem to be any justifiable ground for believing that either of these complaints (erythema pernio and acrocyanosis) is associated with, or consequent on, a calcium deficiency."

As we have stated, a normal calcium level in the blood may give no indication of the behavior of calcium in the body. In our opinion these patients were not given adequate calcium therapy, and we think that definite conclusions as to its efficacy are not warranted.

That irreversible changes in the arterial walls had not developed in any of our cases is shown by the normal appearance of the fingers and toes together with absence of symptoms whenever the surrounding

temperature was above the range in which attacks could occur. During high calcium treatment when the patient was exposed to cold, the symptoms either did not appear or were very much diminished; at higher temperatures the fingers and toes appeared normal, just as they did before calcium treatment. The effect of calcium in these cases is therefore presumably upon the peculiar hypersensitiveness of the blood vessels to cold, and not upon the normal vasomotor nervous control of the vessels.

In this respect the effect of calcium is fundamentally different from that of sympathectomy, which benefits spasmodic arterial disease only indirectly, i. e., by paralyzing the (normal) vasoconstrictor mechanism and so causing permanent vasodilatation. The extremities after sympathectomy are usually distinctly warmer than normal at all atmospheric temperatures, and are consequently less susceptible to the effects of cold. No apparent ill-effect is noted as a result of the loss of the pilomotor and sweating reflexes. Nevertheless, as Lewis emphasizes, the underlying hypersensitiveness to cold of Raynaud's disease persists, and can still be evoked by sufficiently prolonged exposure to cold.[21]

SUMMARY

Four cases are described in which there was spasmodic vascular disease of the Raynaud type characterized by hypersensitiveness to cold. Distinct benefit was obtained by a high-calcium-high-vitamin regime. The effect of calcium differs from that of sympathectomy in that no permanent alteration of the vasomotor nervous mechanism is brought about.

REFERENCES

1. Raynaud, M.: Monograph: De l'Asphyxie Locale et de la Gangrène Symmétrique des Extrémitiés, Riqnoux, Paris, 1862.
2. Gross, L.: J. Path. & Bact. **27**: 27, 1924.
3. Kahn, B. S., and Roe, J. H.: J. A. M. A. **86**: 1761, 1926.
4. Montgomery, D. W., and Culver, G. D.: J. Cutan. Dis. **33**: 119, 1915.
5. Osler, W.: Textbook: Principles and Practice of Medicine, Ed. 10, 1925, D. Appleton & Co., New York City, p. 1146.
6. Mumford, P. B.: Brit. J. Dermat. **37**: 414, 1925.
7. Claude, H., and Tinel, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **49**: 570, 1925.
8. Poulton, E. P.: Lancet **2**: 1282, 1926.
9. Deschamps, P. N.: J. méd. franç. **18**: 251, 1929.
10. Barath, E.: Monograph: Die Experimentellen und Klinischen Grundlagen der Therapie mit Calciumsalzen, Budapest, Königil. Ungar. Universitätsdruckerei, 1931.
11. Margolin, G. S.: Klin. Wehnschr. **5**: 148, 1926.
12. Wright, A. E.: Lancet Jan. 20, 1897, and Layani, Les Acrocyanoses, quoted by Hallam (see below).
13. Lewis, T.: Heart **15**: 7, 1929; and **15**: 229, 1930.
14. Blackader, A. D.: Canad. M. A. J. **21**: 592, 1929.
15. Jaffe, H. L., and Bodansky, A.: J. Exper. Med. **52**: 669, 1930, and Hunter, D., and Aub, J. C.: Quart. J. Med. **20**: 123, 1926.
16. Aub, J. C., Bauer, W., Heath, C., and Ropes, M.: J. Clin. Investigation **7**: 97, 1929.
17. Gunther, L., and Greenberg, D. M.: Arch. Int. Med **47**: 660, 1931.
18. Percival, G. H., and Stewart, C. P.: Brit. J. Dermat. **39**: 115, 1927.
19. Idem: Ibid. **39**: 144, 1927.
20. Hallam, R.: M. Press **129**: 408, 1930.
21. Adson, A. W., and Brown, G. E.: J. A. M. A. **84**: 1908, 1925; and Davis and Kanavel: Surg. Gynec. & Obst., **42**: 729, 1926, quoted by Lewis, and Lewis, T.: Heart **15**: 7, 1929.

VENTRICULAR BIGEMINY (PARASYSTOLE OR RECIPROCAL RHYTHM) IN ATRIOVENTRICULAR RHYTHM*

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CASES of atrioventricular rhythm with a certain type of ventricular bigeminy have been reported from time to time for many years. The electrocardiograms are characterized by conspicuous variation in the P-R and R-P intervals and by premature beats occurring at short intervals after the rhythmic ventricular contractions. The premature beat is not followed by a compensatory pause and it is preceded, in most of the reported cases, by a more or less well-defined P-wave. Authors who have reported such cases have employed two different theories to account for the second of the bigeminal beats. Both theories agree that the causative impulse is supraventricular in origin, but they differ regarding its exact site of origin and its character.

The advocates of the theory of *reciprocal rhythm* regard all auricular activity in these cases as due to impulses which originate in the A-V node. The cases differ from other instances of atrioventricular rhythm, however, in that the conduction of impulses from the A-V node *backward* to the auricle is interfered with. Contraction of the auricle consequently occurs at an interval after ventricular systole which grows progressively longer; i.e., the R-P interval increases. Conduction of the nodal impulses downward to the ventricle, on the other hand, is unimpeded, and this chamber responds without delay. But ventricular activity is not limited to the rhythmic impulses coming directly from the node. When the lengthening R-P interval reaches a certain value, a premature ventricular contraction occurs in response to an impulse from the auricle. By some it is supposed that the contraction of the auricle, set off by the nodal impulse, itself constitutes the stimulus to the premature ventricular systole. By others it is suggested that the nodal impulse in some way returns from the auricle, passing again through the A-V tissue and thus reaching the ventricle by a sort of circulating mechanism. In support of this notion its proponents cite Mines' classical experiment with the heart of a tortoise; an experiment, it will be recalled, which was concerned not with atrioventricular rhythm but with movement around a ring composed of both auricular and ventricular tissue.

Those who invoke the theory of *parasystole* believe that the auricular activity is due to impulses which originate, not in the A-V node, but at an independent pacemaker in the auricle. The rate of the auricular pacemaker is slower than that of the nodal pacemaker, and the progressive lengthening of the R-P interval results from this difference in rates. Under this theory, as well as under the other, *interference to the conduction of impulses from the A-V node to the auricle is assumed.* The interference, however, must be complete, thus guarding the center of slower rate from the faster center. But the block must apply to the passage of impulses only toward the auricle and not toward the ventricle. It must be unidirectional. For if impulses from the slower center were prevented from reaching the ventricle they could not excite it, and the resulting mechanism would constitute not parasystole but A-V dissociation. But since the block is only in the one direction, impulses elaborated at the auricular center as well as those from the A-V node pass toward

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the ventricle and themselves produce responses when not prevented by refractory tissue. Such ventricular responses to impulses from the auricular center, occurring before the sequential rhythmic impulse from the lower center is due at the ventricle, produce interruptions to the dominant ventricular rhythm.

Under both theories these cases are regarded as examples of socalled A-V rhythm in which the regular beating of the ventricle is interrupted by another supraventricular impulse whenever it finds the lower tissues responsive. One theory holds that both the auricle and the ventricle are activated from a single center located between them; asynchronism in contraction depending on unidirectional impairment in conduction. Under the other theory the auricle is activated from a center separate from that which activates the ventricle; asynchronism resulting from difference in the rates of the auricular and ventricular centers.

Before pursuing further the particular problem involved in the special cases of A-V rhythm with which this paper is concerned, brief consideration must be given to A-V rhythm itself. This name is given to a phenomenon produced under certain experimental conditions, particularly by destruction of the S-A node or by stimulation of the right vagus and the left sympathetic nerves. Under such circumstances the electrocardiographic complex of ventricular activity is not preceded by the usual form of P-wave at the usual interval. The P-wave is usually, but by no means invariably, inverted (Scherf and Shookhoff). Clinical electrocardiograms of similar form are similarly designated.

It is usually assumed, in explanation of such records both experimental and clinical, that a single focus somewhere in the A-V node has become the pacemaker and that impulses from it pass both to the auricle and to the ventricle. It is commonly held that different areas of the node may become such new centers of impulse formation, but orthodox opinion usually limits this to a single focus at a given moment and confines that center to the A-V node.

Geraudel has presented certain conceptions of impulse formation and transmission within the auricle, however, to which consideration must be given in any attempt to explain the mechanism of socalled A-V rhythm. He holds that there are several auricular centers which, developmentally considered, are natural areas of impulse formation; such areas not being embraced within the anatomical confines of the A-V node. Such a conception offers ready explanation of certain phenomena associated with A-V rhythm which are difficult to explain on the assumption that the node itself is the precise area of impulse formation. It explains also the different and varying shapes of the P-waves exhibited in experimental and clinical cases of A-V rhythm.

While it is agreed that suppression of the normal pacemaker produces "escape" from that area whose rhythmicity (or automaticity) is next in degree to that of the sinus, there is much evidence that this new pacemaker need not necessarily be within the A-V node, but that it may be at any one of several areas. Further suppression may dislocate the pacemaker to still another area. In the case of supraventricular extrasystoles it is indeed difficult in many instances to know whether the abnormal P-waves recorded in the electrocardiogram represent "nodal" or "auricular" extrasystoles and the difference between the two is growing less distinct.

The conception of A-V nodal rhythm which appears best to accord with experimental data is as follows: Under circumstances which depress impulse formation at the normal (sinus) area, another supraventricular area of impulse formation escapes. Further depression may suppress the second area and uncover another. That supraventricular area, in any case, whose automaticity at the moment is highest, becomes

the pacemaker. Rhythmic impulses originating in this pacemaker pass both toward the auricle and toward the ventricle. If conduction is unimpaired, both chambers respond to each rhythmic impulse. Other supraventricular areas of impulse formation then begin to build up impulses but are discharged before the completion of their rhythmic periods; the whole auricle as well as the ventricle responding to impulses from the dominant area. The location of this dominant area need not necessarily be within the A-V node in every case, the conception that it is so located having been based more upon assumption than upon experimental evidence. In many instances the new pacemaker appears to be "auricular" rather than "nodal." We employ the term atrioventricular rhythm with this conception, one somewhat broader, perhaps, than that usually implied by the term.

We have applied the theories of parasystole and of reciprocal rhythm to ten cases of atrioventricular rhythm of the particular type under discussion. The data in these cases collectively and in detail appear to elucidate the problem of mechanism. Study of them as a group reveals much evidence of intimate relationship between A-V rhythm, parasystole, and so-called reciprocal rhythm. The three rhythms appear to depend upon the same fundamental factors, the exact mechanism in different instances being determined by incidental differences in retrograde conduction from the dominant area. Just as a certain modification of retrograde conduction changes simple A-V rhythm into parasystole, so a different modification of retrograde conduction may produce that mechanism which has been called reciprocal rhythm. This conception will be elaborated after presentation of certain records by which it is strongly indicated. The cases not reported in this paper support the conception outlined above and might well be presented except for lack of space.

REPORT OF CASES AND DESCRIPTION OF ELECTROCARDIOGRAMS

CASE 1.—A white man of twenty-nine years was admitted to the Barnes Hospital, October 17, 1926, complaining of defective vision and headaches. There had been head trauma two months before admission. The past history was negative with regard to his heart. At examination it was noted that the area of cardiac dullness was slightly enlarged and that there was a systolic murmur at the apex, heard also over the precordium. The heart beats occurred in pairs. On October 25, 1926, a large endothelioma was removed from the left temporal region. During the operation his heart beat regularly. The patient made an uneventful recovery.

Electrocardiograms were made on October 18, 19, 21, during operation on October 25, and on November 6, 1926. Upon two of these occasions records were made following the intravenous administration of atropine sulphate in doses of 1/50 of a grain and 1/25 of a grain respectively.

The records are of four types. Specimens of each are shown in Figs. 1 and 2. In Fig. 1 we have indicated our conception of the mechanism by the drawings below the electrocardiograms. The record shown in the upper left-hand part of Fig. 1 was made during operation. The mechanism is normal and the area of

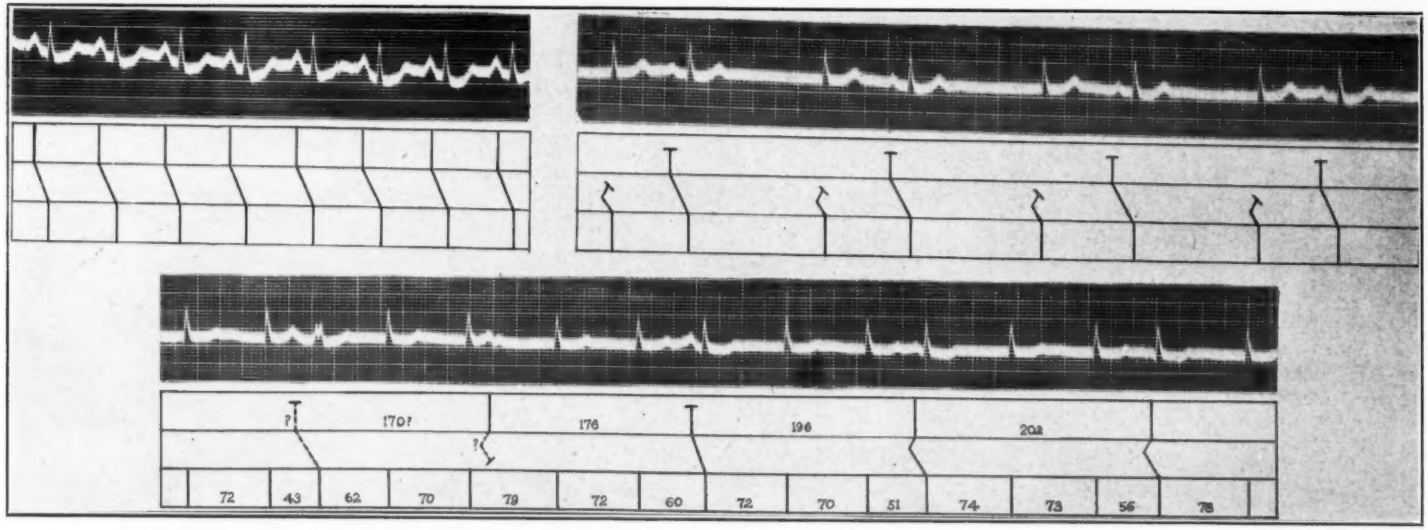

Fig. 1.—Electrocardiograms of the patient in Case 1. At the left of the top strip is the record in Lead II made at operation October 25, 1926. At the right of the top strip is the record in Lead II made October 19, 1926. This is similar to the admission record, but is clearer, and on that account is reproduced instead of the admission record. The bottom strip is the record in Lead II made October 19, 1926, two and one-half minutes after the administration of 1/50 grain of atropine.

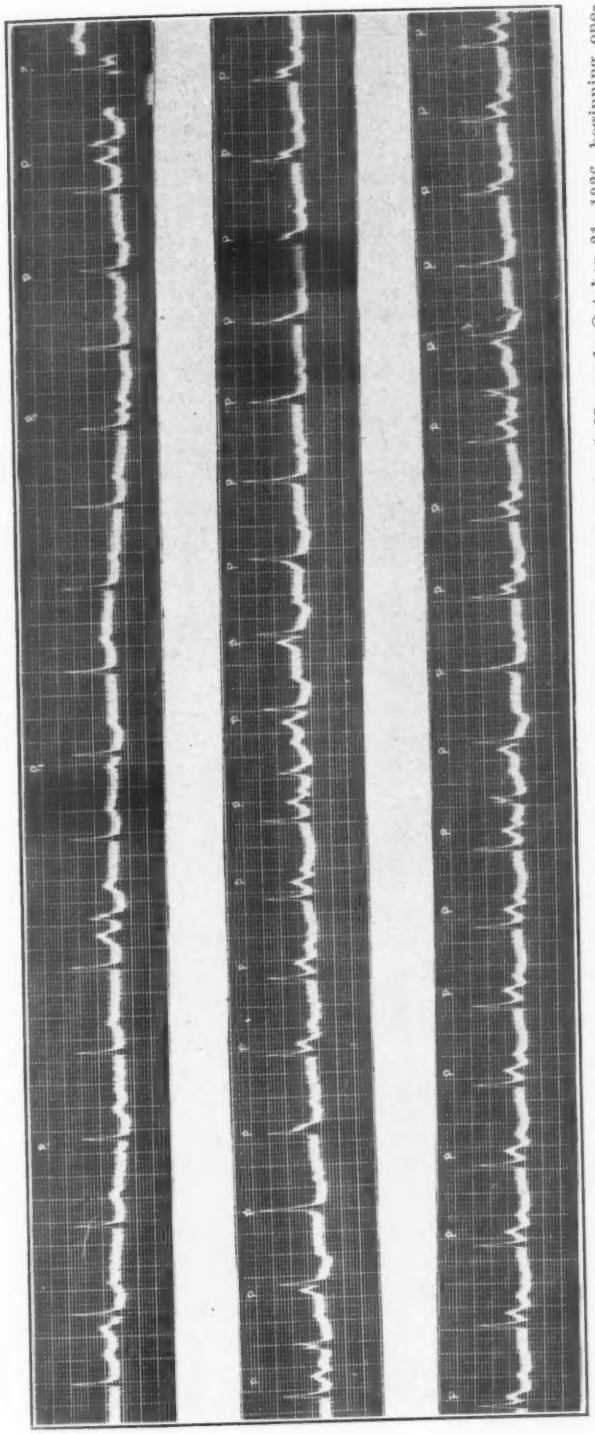

Fig. 2.—Electrocardiograms of the patient in Case 1. This is a continuous record in Lead II, made October 21, 1926, beginning one-half minute after the administration of 1/25 grain of atropine. Note the different shapes of the P-waves in the first part, and the rhythmic (large) P-waves in the last part. Note also the aberrant ventricular complexes following those P-waves which are properly spaced after P-waves.

impulse formation presumably is the sinus region. The electrocardiogram in the upper right-hand part of Fig. 1 is a record of the same type as the admission record. It shows ventricular complexes occurring in pairs, the first unaccompanied by an auricular wave but the second preceded by one at a constant interval. This P-wave is upright but its shape is different from that in the electrocardiogram made during operation in which the sinus P-wave appears to be depicted.

Effect of Atropine.—The last strip of Fig. 1 was recorded two and one-half minutes after 1/50 of a grain of atropine. Several P-waves with shapes different from that in the control and with short P-R intervals appear. Fig. 2 is a continuous record beginning 30 seconds after the administration of 1/25 grain of atropine. In the first part P-waves of two types are recorded. Those which predominate are similar to the ones recorded after the smaller dose of atropine. The others, which are larger, during the early effect of atropine occur only at rather long intervals, but under complete atropine effect they constitute the only type recorded. During the last 30 minutes of the atropine experiment they occurred regularly, and at a rate of 85 per minute. They are similar to the P-wave in the record made at operation and appear to represent activity originating at the normal pacemaker, while the smaller P-waves represent secondary pacemakers.

We interpret the second strip in Fig. 1 as follows: It records an independent ventricular rhythm with retrograde block between the ventricular* pacemaker and the auricle. The degree of vagus stimulation responsible for this mechanism was sufficient to suppress the normal pacemaker. The auricle, therefore, receiving stimuli neither from the ventricular pacemaker nor from the sinus area, escaped at a secondary center. Impulses from this secondary area were conducted to the ventricle, exciting it to contraction. This constitutes true parasystole, the ventricle being activated by impulses both from the ventricular and from the secondary pacemakers.

The effect of small amounts of atropine was enough to uncover other secondary centers of impulse formation, but the full effect was required to uncover the sinus pacemaker. Atropine not only lessened vagus tone at the sinus area, but it accelerated the ventricular pacemaker as well, so that under its effect the rate of the ventricle still was faster than that of the auricle. Although at operation the sinus pacemaker dominated the rhythm, under 1/25 of a grain of atropine parasystole still obtained, the ventricular responses to impulses from the auricular center showing aberrant complexes. It will be noted that the pause following the aberrant ventricular complex is somewhat shortened. The explanation of this short interval has been given by Scherf and Shookhoff. They explain it as due to impairment of conductivity in the lower tissues resulting from the premature passage of the auricular impulse. This impulse is transmitted before the tissues have had sufficient rest and because of the accompanying conduction defect the P-R interval

*In the following pages the center of impulse formation from which the ventricle is activated will be referred to as the "ventricular pacemaker," that which activates the auricle as the "auricular pacemaker." By such designations we do not imply that these natural areas of impulse formation are located in the chambers activated by them.

The term "retrograde" as applied to the conduction of impulses will be used to mean conduction in a direction other than toward the ventricle. Retrograde conduction, therefore, is necessary in order for an impulse from the ventricular center to reach any secondary (and slower) center of impulse formation.

associated with the premature beat is prolonged. The aberrant complex, therefore, is set further to the right than it would be if conduction were at a normal rate, the following interval thus being encroached upon.*

This incomplete recovery accounts also for the slight difference in shape shown by the T-waves of the ventricular complexes which follow the aberrant beat.

The fact that the auricular waves occur rhythmically and that this rhythm is undisturbed even in connection with the premature beat argues in favor of an independent auricular pacemaker. Inspection of this record alone, however, could hardly lead to a conclusion in the matter. But study of the case as a whole presents evidence which appears to admit of no other interpretation. The pairing of the ventricular beats recorded in the admission record (upper right of Fig. 1) could hardly be explained on the basis of so-called reciprocal rhythm. Such an assumption would meet difficulty in the long R-P intervals. The conclusion that the auricle is activated from a center or from several centers which are independent of the ventricular pacemaker is supported also by the variations in the shape of the P-waves which appear not only in different records but also in different parts of the same record. These variations would be hard to explain on the basis of difference in retrograde conductivity from a single pacemaker common to both ventricle and auricle.

Summary of Case I.—A case in which sinus depression resulted in escape at a secondary center. Impulses from this secondary center activated the ventricle but were not conducted to the auricle. The location of the pacemaker for the auricle varied, changing with vagus (and sympathetic) tone under such circumstances as a cerebral operation and the administration of atropine. Impulses from these various auricular centers, conducted to the ventricle, produced ventricular contractions when favorably timed, the response of the ventricle to such auricular areas as well as to the rhythmic ventricular center constituting parasystole.

CASE 2.—A colored man, aged sixty years, came to the Washington University Dispensary, February 2, 1928, complaining of increasing dyspnea, edema of the ankles and paroxysms of nocturnal dyspnea. Examination revealed emphysema, tortuous and sclerosed radial arteries, faint heart sounds and gallop rhythm. The rate was 80 per minute. There was no arrhythmia. The outline of cardiac dullness was ill-defined but it appeared to be somewhat increased to the left. The Wassermann reaction was negative. The blood pressure was 160/70. He had been taking digitalis, but the exact amount was not recorded. The tincture was then ordered, 15 drops three times a day. There was at first some general clinical improvement but this was followed by an increase in the number of attacks of nocturnal dyspnea. He returned to the dispensary at intervals until June 14, 1928, there being no notable clinical change during this period.

*In some cases conduction has not fully recovered by the time of the next R-R interval and this also is slightly abbreviated.

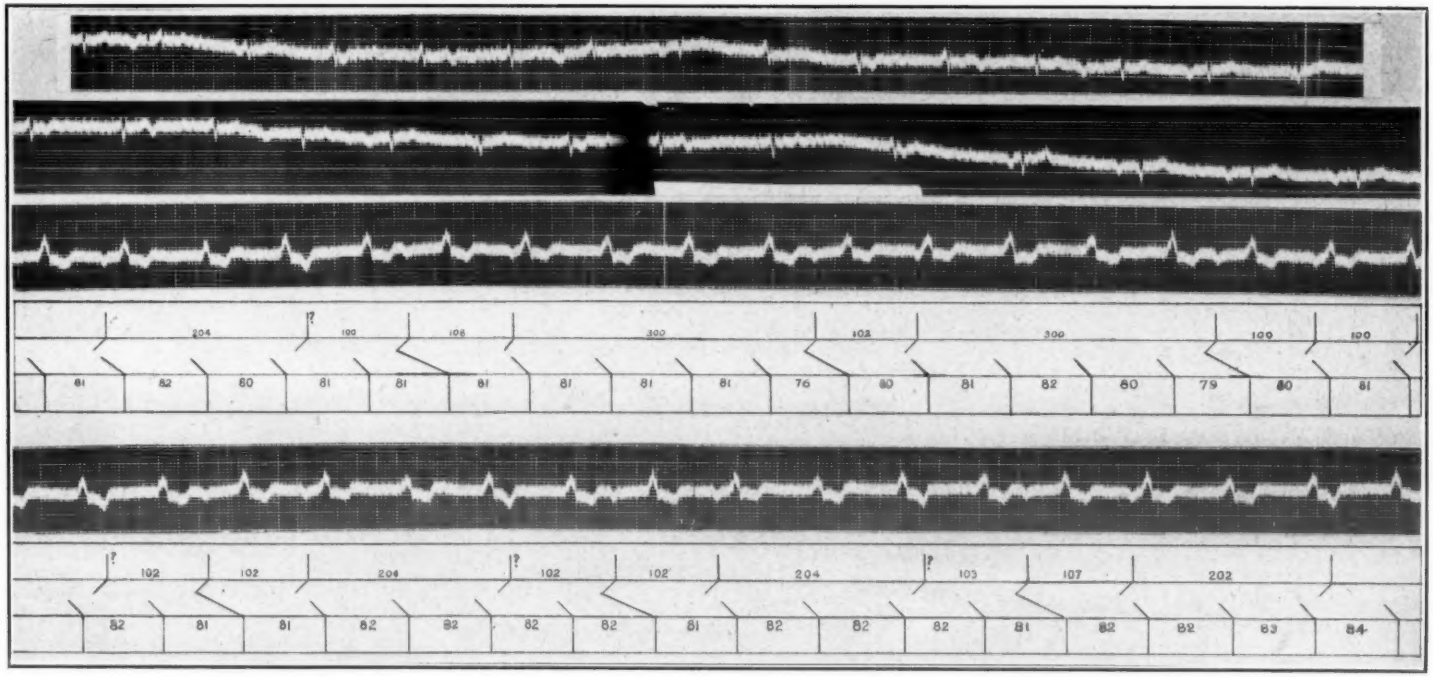

Fig. 3.—Electrocardiograms of the patient in Case 2, made June 9, 1928. The first and second strips are records in Lead III showing the effects of pressure over the right and left carotids, respectively. In the second strip the time of pressure is indicated by the signal at the bottom. In the first strip the pressure was applied just before the beginning of the fifth R-wave. The third and fourth strips are a continuous record in Lead II. Discussion in the text.

Fig. 4.—Electrocardiograms of the patient in Case 2. Lead II, June 14, 1928. The first and second strips are continuous. Note the progressive change in the position of the P-wave without notable arrhythmia. In the third strip note the short P-P interval coincident with the short R-R interval in the last third of the record. Discussion in the text.

Electrocardiograms were made upon five occasions. In the first two (February 2 and April 26) no arrhythmia is recorded, the P-waves are of normal shape and each is followed by a ventricular complex at a normal interval (0.17 of a second). In later records, parts of which are reproduced, the P-waves are of different shape and the normal P-R relationship does not obtain. The top strip of Fig. 3 is a record (June 9) in Lead III with pressure over the right carotid. It appears to show complete or almost complete dissociation between auricle and ventricle, the rate of neither having been affected by carotid pressure. Pressure over the left carotid, recorded in the second strip, caused a slowing of the ventricle but had little effect on the rate of the auricle. It will be observed that the rate of the ventricle (before carotid pressure) is 70-73, while that of the auricle is only 58-60. It will be noted further that the P-waves are inverted not only in Lead III but also in Lead II (third and fourth strips).

The first and second strips of Fig. 4 constitute a continuous record in Lead II made June 14. They are a part of a long record which shows a variation in ventricular rate from 62 to 71 and a variation in auricular rate from 58 to 65. At the beginning of the top strip the ventricular rate is 64 and no P-waves are clearly visible. P-waves soon appear, however, as notches on the right of the R-waves; and near the end of the top strip a definite T-P interval has developed, showing clearly defined P-waves with a rate of about 60. In the second strip this T-P interval increases progressively until the P-wave is lost in the succeeding R complex after which it emerges to the right of the *second* R-wave; all this without conspicuous arrhythmia either of the R- or of the P-waves. The ventricular rate in the second strip is about 62.

The A-V dissociation with the rate of the ventricle higher than that of the auricle, the regularity of the auricle with change in ventricular rate, and the abnormal shape of the auricular complexes appear to necessitate the following interpretation of the first and second strips of Fig. 3: Depression of the normal pacemaker with ventricular escape; retrograde block from the ventricular pacemaker, resulting in auricular escape at a secondary center; downward block from this secondary auricular pacemaker protecting the ventricular center from its impulses. This two-way block produces complete A-V dissociation.

It should be noted that this case presents two features in which it differs from the usual case of A-V block; the ventricular rate is relatively high and the P-waves are inverted. The first of these features is explained by the mechanism of origin. Socalled A-V rhythm owes its inception to just such an abnormal relationship between the rate of the normal pacemaker and that of a secondary center. The second feature which differentiates this case from simple A-V block, i.e., the inverted P-waves, depends upon two factors. One of these also is inherent in its origin; the sinus area regularly is depressed in cases of this sort. The second is the distinguishing feature: the conduction of impulses backward from the ventricular center is blocked. Under such circumstances sinus depression leads to auricular escape at a secondary center.

Upon occasion one center may activate both chambers. It appears that the temporary improvement of conduction responsible for this phenomenon is always an improvement from auricle to ventricle, never

in the reverse direction. Removal of downward block at certain intervals is shown in the third and fourth strips of Fig. 3. These two strips are a continuous record in Lead II. In them a certain sequence is recorded again and again without variation; a P-wave stands about midway between two R-waves; in the next cycle it stands to the left of the R-wave; in the third cycle it is lost; in the fourth it modifies the T-wave, and in the fifth it appears again in the same position as at first. In a long record this sequence is unvarying and the conclusion is inescapable that the auricular and ventricular complexes in some way are related. The nature of this relationship is explained by further study of the record. It will be observed that the R-R interval associated with the long P-R interval frequently is short.* Slight variations in rate are common both to the auricle and to the ventricle. If these short R-R intervals should be found to occur with synchronous changes in auricular rate, either might be thought to depend upon the other, or both might depend upon a common factor. But they are not so associated. Irrespective of the attendant auricular rate, the interventricular interval under consideration never is long: either it is short, or its length is not affected. This short interventricular interval is related, therefore, not to auricular rate, but to that particular auricular complex whose position in relation to it is constant. Every fifth auricular complex has this relationship and the conclusion follows that every fifth auricular impulse produces a ventricular contraction. These ventricular responses to auricular stimuli occur, however, only a little before the completion of the rhythmic ventricular periods, producing only slight shortening of the associated interventricular intervals. This results from the fact that the conduction defect is of considerable extent.

Instead of this relief of downward block occurring rhythmically as in Fig. 3, occasionally it occurs only in isolated instances. In the first strip of Fig. 3 the sixth interventricular interval appears to be an example. It is a little shorter than the others and in it a P-wave is situated in about the same relative position as the P-waves in the last strip that are associated with conducted auricular impulses. Another instance which gives better evidence of the occasional downward conduction of auricular impulses is shown in the bottom strip of Fig. 4. The fourth from the last interventricular interval is short. The associated interauricular interval also is short, and the shape of the P-wave which closes it differs slightly from that of the preceding P-waves. It is probable that this P-wave represents auricular response to an impulse originating at an area different from that which had been activating the auricle, and that this impulse also reached the ventricle.

Attention has been called to the fact that slight variations in rate

*This is well shown in the tenth R-R interval of the third strip, resulting there in a definite, though not conspicuous, ventricular bigeminy.

occur at both the auricular and the ventricular pacemakers. In portions of some of the records in which the interpretation is equivocal it is probable that the uncertainty is due to a changed relationship between the rates of the two pacemakers rather than to a change in mechanism. Fig. 4 is a case in point.

The second part of this record (middle strip of Fig. 4) would appear to admit of only one interpretation, viz., independent auricular and ventricular pacemakers with rates almost identical, but with the rate of the ventricular center a little faster than the other. In the first strip, however, the alternative explanation of a single pacemaker for both auricle and ventricle must be considered. If the first part were studied alone, the temporary absence of visible P-waves and the nearly identical rates of auricle and ventricle might favor that interpretation. It is conceivable that temporary improvement in conduction might have allowed one pacemaker for a short time to activate both chambers. But study of the whole record (as well as other records in the case) suggests change in rate rather than change in conduction as the correct explanation of the difference between the two parts of the record, and indicates that the beginning as well as the following parts of the record in Fig. 4 represents separate auricular and ventricular pacemakers. The rates of the two pacemakers are not far apart to begin with and only a slight change of either would be required to make them nearly identical. In Fig. 4 the difference between the rates of the auricle and the ventricle is not as conspicuous as it is in Fig. 3. It is on this account that the interpretation of mechanism is less readily apparent in Fig. 4.

Summary of Case 2.—A case of sinus depression with ventricular rhythm, impulses from the ventricular center failing to reach the auricle. The depression of the normal pacemaker is of such extent that auricular escape occurs at a secondary area. Not only is retrograde conduction from the ventricular center depressed but there is also such impairment of downward conduction from the secondary auricular area that its impulses rarely reach the ventricular center. The result is almost complete dissociation between the secondary auricular and the ventricular centers, the ventricle being activated only rarely by impulses from the auricular center.

CASE 3.—A colored woman, forty-two years of age, was admitted to the Barnes Hospital, December 15, 1926, complaining of dyspnea and cough. Nine years previously she had had some sort of acute arthritis. The dyspnea was of several years' duration and for a few months she had been incapacitated. She had been taking 60 drops of tincture of digitalis daily for ten weeks before admission. Examination revealed generalized edema, an enlarged liver, and diminished breath sounds over the right base of the chest. The heart was conspicuously enlarged to the left and both a systolic and a diastolic murmur were heard over the precordium. Extrasystoles were noted. The systolic blood pressure was 125, the diastolic, 55 mm. The Wassermann reaction was positive. Following a short period of improvement

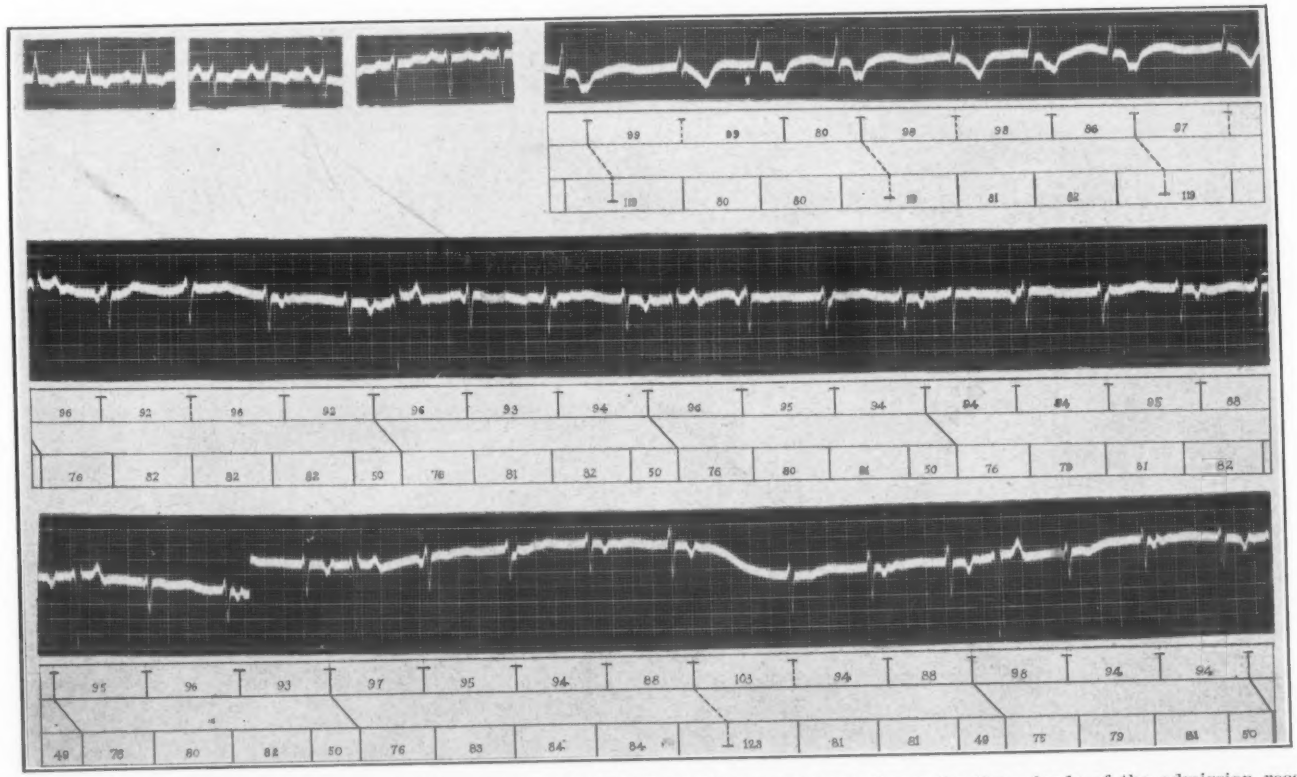

Fig. 5.—Electrocardiograms of the patient in Case 3. At the left of the top strip are shown the three leads of the admission record; at the right is the record in Lead I made December 29, 1926. The middle and last strips are a continuous record in Lead III made December 30, 1926. Discussion in the text.

she became worse and after a variable course she died March 3, 1927. Postmortem examination revealed a thrombus adherent to the wall of the right auricle, hypertrophy and dilatation of the heart and syphilitic disease of the aorta and of the aortic valves.

Electrocardiograms were made upon five occasions. The one made upon admission (Fig. 5, upper left part) shows no abnormal rhythm, but later records show the independent ventricular rhythm, inverted P-waves and premature ventricular complexes characteristically situated (see middle strip of Fig. 5), features which put them in the category under discussion.

From the evidence presented in Cases 1 and 2 and which will be elaborated below, this case appears to be an instance of parasystole involving ventricular and secondary auricular pacemakers. It is presented because of two additional features not shown in the other cases. One appears to have no bearing upon the general problem of mechanism but offers important evidence upon a related question. It consists in a certain modification of ventricular rhythm as follows: In some of the places where the premature beat regularly occurs none is recorded, but the location of the following ventricular complex is exactly what it would have been had the premature beat occurred. (See bottom strip of Fig. 5.) Comment upon this modification of ventricular rhythm will be reserved for a subsequent footnote.

The other special feature of this case, however, furnishes evidence of great importance to the problem with which this paper deals. It relates to the auricular rhythm. The basic rhythm of the auricle in this, as in other cases, shows slight variations. The interauricular intervals vary between 0.92 of a second and 0.96 of a second (middle strip of Fig. 5). Upon occasion, however, that interval which precedes the break in ventricular rhythm is shortened, an interval of 0.88 of a second being recorded in three instances. Upon other occasions slight shortening of this interval is suggested, but in view of the arrhythmia throughout the record, no such special feature in these other instances can be demonstrated.

The P-waves which close these short intervals and whose early occurrence is responsible for the abbreviation, have a characteristic position. They occur at about 0.20-0.22 of a second after the beginning of the preceding R-wave. P-waves which occur earlier with reference to R-waves never are premature. In other words, whenever the rhythmic occurrence of an auricular complex would place it nearer to the R-wave than 0.20 of a second, it falls at its rhythmic interval. But if the completion of its rhythmic interval would cause it to fall at a time after R greater than 0.22 of a second, it occurs prematurely. In occurring prematurely, moreover, it is never closer to R than 0.20 of a second. This invariable relationship to the preceding ventricular beat can hardly be fortuitous. The simplest explanation, and indeed the only one that appears to us at all probable, is that the impulse from the ventricular center discharges the auricular pacemaker if it arrives at the time when

the auricular stimulus is about to be spontaneously discharged. That it does not thus affect the auricular center in the cases of those P-waves which are inscribed earlier with reference to R and 0.20 of a second indicates that the conduction of the impulse backward from the ventricular pacemaker is impaired.*

When the auricular pacemaker is discharged prematurely one would expect the length of the following P-P interval to be unaffected. In certain instances such is the case (e.g., at the beginning of the bottom strip of Fig. 5. See also upper right-hand strip at top of Fig. 5). Upon other occasions, however, it is somewhat prolonged and this lengthened period requires explanation. In such instances it is possible that the early occurrence of the auricular beat is due to the elaboration of a stimulus at a secondary center of impulse formation, a phenomenon recorded in some of our other cases. What appears to be probable, however, is that such a secondary center located near the dominant auricular pacemaker has been discharged by the impulse from the ventricular pacemaker. This explanation is supported by the fact that even in such instances the position of premature P-waves with reference to the preceding R-wave is the same as upon other occasions.

The impulse which is prematurely discharged produces an auricular contraction and passes toward the ventricle just as do other impulses from the auricular pacemaker. Unless its passage is interfered with it elicits a ventricular contraction. As in the case of the rhythmic impulses, whether or not it does so depends upon the time relationship of its occurrence to events below it. If it finds the lower tissues responsive a premature ventricular beat occurs.

The premature auricular impulse which is shown above the broken diagonal line near the middle of the diagram accompanying the lowest strip in Fig. 5 does not elicit a ventricular response. But although the ventricle fails to beat in response to this auricular impulse, the next beat of the ventricle takes place not after the rhythmic interventricular interval but at that time when it would have occurred had a ventricular contraction followed the auricular impulse. *The ventricular pacemaker appears to have been discharged* without effecting a contraction of the ventricle.† The same phenomenon is recorded regularly in the right-hand part of the top strip of Fig. 5.

Our explanation of the occasional short P-P interval as due to incomplete retrograde block from the ventricular center cannot be proved.

*This paper is not primarily concerned with theories of block. Whether impulses from the ventricular pacemaker fail to excite the auricular center on these other occasions because they do not reach it, or because upon arrival they find it less responsive, we do not attempt to say.

†Much has been written regarding the site of delay and of block in cases which exhibit a prolonged P-R time or a failure of ventricular response to an auricular impulse. The evidence in our records just referred to supports the contention of Scherf and Shookhoff that the block is in the tissues of the A-V bundle below the A-V node. Or rather in our case it is below the ventricular center of impulse formation. This deduction follows from inspection of the record. Attention has been directed to the fact that the interventricular interval following the premature ventricular beat is not prolonged. This results from the discharge of the ventricular pacemaker by the passage through it of the auricular impulse. After its discharge the ventricular center elaborates another impulse at its regular interval. Upon this all authors are in agreement. The records in Fig. 5 indicate, however, that although the ventricular center was discharged by the auricular impulse, *no ventricular response was elicited*. The sequence of events in this part of the curve is exactly the same as it is in analogous parts except that the QRS complex is missing. If the auricular impulse discharged the ventricular center, therefore, and yet did not excite the ventricle, the failure of ventricular response was due to incomplete recovery of tissues below the center. While this feature of the case has no direct bearing upon the question at issue in this paper, it is, so far as we are aware, a unique record and because of its apparent bearing upon the problem of block it is reproduced.

Those who have interpreted such records on the basis of reciprocal rhythm explain not only the premature auricular impulse, but all others as well, as originating in the ventricular center. This record alone cannot disprove such a theory. Both the theory of a single pacemaker and that of dual pacemakers assume a conduction defect from the ventricular pacemaker to the auricle. As applied to this record, however, the conception of a single pacemaker necessitates the assumption of a sort of haphazard change in conductivity in order to explain the auricular arrhythmia. The theory of dual pacemakers explains the auricular arrhythmia as due to the mathematical relationship between the time of arrival of the (retarded) impulse and the rhythmic period of the auricular pacemaker. The agreement of this explanation with recognized physiological principles and the general similarity of the records in this case to those in other cases in which two pacemakers appear to be demonstrated will be presented as evidence favoring the conception that these cases of so-called reciprocal rhythm are but modified forms of parasystole.

Summary of Case 3.—A case of sinus depression with ventricular rhythm and impairment of retrograde conduction from the ventricular center. The guarding of the auricular pacemaker from the ventricular center was not quite complete, and occasionally the elaboration of an auricular impulse was hastened by the arrival of a stimulus from the ventricular pacemaker. The ventricle responded to auricular impulses unless prevented by refractory tissue, such responses together with those from the ventricular center constituting parasystole.

GENERAL DISCUSSION

The modification of simple atrioventricular rhythm which produces the mechanism shown in the cases of this group can be fully appreciated only in its relationship to the fundamental mechanism of uncomplicated cases. Atrioventricular rhythm originates under conditions which depress the sinus area or which exalt another center of impulse formation; or under conditions which produce both effects. The result is that secondary centers of stimulus production are uncovered. That center whose automaticity is highest will dominate all others, in the manner described above, provided impulses from it are freely conducted to them. Impulses from the dominant area, under such circumstances, activate both the auricle and the ventricle. Such a case, with no impairment of conductivity, falls into the category of simple atrioventricular rhythm.

If there is a defect in retrograde conduction, however, a modification of this simple mechanism results. Impulses from the dominant area, in some cases, while freely conducted to the ventricle, are not conducted to the auricle. There is retrograde block. Under such circumstances the auricular center of impulse formation whose degree of automaticity

is next in order escapes,* and impulses *from it* activate the auricle. Just which of the natural centers of impulse formation will become the pacemaker for the auricle in a given case depends upon circumstances.** In one case it may be the sinus area (Case 1); in other instances sinus depression may lead to escape at a lower center (Cases 2 and 3). The shape of the P-waves, therefore, will differ in electrocardiograms of different cases. In an individual case, moreover, changes in vagus tone may depress that area which has been dominant and uncover another. The shape of the P-waves, therefore, may vary in the same record (Case 1). The rate of such a secondary auricular center is necessarily slower than that of the ventricular center; for if it were not slower this auricular center itself would have assumed the rôle of pacemaker and its impulses would dominate the ventricular rhythm. The blocking between the two centers in most instances, moreover, is only in the one direction, impulses from the secondary center being conducted to the dominant center and discharging it prematurely when not prevented by refractory tissue. Such cases fall into the category of parasystole.

It will be observed that the difference between cases of A-V rhythm which exhibit parasystole and those which do not is a difference in the retrograde conduction of impulses from the ventricular pacemaker. In one class of cases impulses are readily conducted backward, in the other they are blocked. There may be intermediate stages of retrograde conductivity, however, corresponding to well-known differences in downward conductivity. In certain cases the impairment, while considerable, is not complete (Case 3). There is partial retrograde block. In such a case the dominant auricular center will discharge its impulses rhythmically when it is undisturbed by impulses from the faster center. Under certain circumstances, however, it may be discharged prematurely by the arrival of an impulse from the ventricular center. This occurs only when the ventricular impulse reaches the auricular center near the end of its automatic period.† The impulse from the auricular pacemaker, when prematurely discharged, spreads exactly as it does when automatically released, activating the auricle and, unless interfered with, the ventricle as well. In such cases the impairment of conductivity from the faster center to the slower, while sufficient to prevent the one from dominating the other completely and thus establishing simple A-V rhythm, is yet not great enough to allow the develop-

*"Escape" from a natural center of impulse formation is a well recognized phenomenon. It can occur from a center whose rate is below that of the dominant area only when the slower center is protected from the faster. It explains the origin of the ventricular impulses in cases of ordinary A-V block. In such cases it is the ventricular center which is protected from a faster area. The protecting block, moreover, is in the reverse direction, i.e., downward block. In complete heart-block (A-V dissociation) there is, of course, upward block as well. Otherwise the auricular pacemaker would occasionally be discharged by impulses from below and auricular parasystole would result.

**Muscular lesions as well as vagus tone may be important factors.

†The same phenomenon has been observed in certain cases of partial A-V block, dissociation being almost but not quite complete. Although an independent ventricular rhythm may have been established, the ventricle occasionally may beat in advance of its rhythmic period in response to such auricular impulses as arrive just before the automatic ventricular impulse has matured.

ment of pure parasystole. The resulting mechanism stands between these. It is a modified form of parasystole. It depends upon the discharge of impulses not from a single pacemaker but from two pacemakers. When bigeminal beating of the ventricle occurs in such instances, the second beat is in response to an impulse whose immediate origin is different in place but similar in character to that which excites the first beat.

It is the occurrence of premature ventricular beats associated with interauricular intervals thus abbreviated, in cases of atrioventricular rhythm, that has fortified the arguments of those who explain not only these but other instances of bigeminy in A-V rhythm as due to "reciprocal rhythm." The dependence of the second beat upon the first is indicated by the constant relationship between them and the conclusion that the first beat is "in some way" responsible for the second is a sound one. The further conclusion that the auricle is concerned in the causation of the second beat also is sound. But neither the deduction that the *original impulse* which causes the first beat again returns to the ventricle, nor the assumption that it is the stimulus of auricular systole, *auricular contraction itself*, which produces the second beat appears to us to be warranted. Such conceptions imply either that the impulse causing the second beat is identical with that concerned with the first in point of origin or that it differs from it in character. Neither proposition appears to be supported by theoretical considerations, by experimental evidence or by clinical records.

That an impulse enters the auricle by a certain path, proceeds in some unknown way, returns to its point of entry and then proceeds again over the same path of entry but in opposite direction . . . . all this should not be hypothecated simply because under certain experimental conditions instances of circulating mechanism involving a known path have been observed. The hypotheses requisite for an explanation of the premature beat on the basis of parasystole, on the other hand, accord with recognized physiological concepts. Different degrees of conductivity backward as well as forward; separate areas of stimulus production; escape from one of these areas; the anticipation of a rhythmic beat by a stimulus from another center; none of these postulates is at variance with established conceptions of cardiac mechanism. Cases of parasystole, furthermore, are on record, in which the interpretation is unequivocal. Few, if any, of the cases reported as "reciprocal rhythm" appear to necessitate such a separate interpretation.

A comparative study of the records in our cases strongly indicates that the mechanism in these instances in which short P-P intervals are associated with the premature ventricular beats is fundamentally the same as that which obtains in cases with no auricular arrhythmia. This conclusion is indicated both by the general similarity between the two kinds of records and by the fact that in a single record both phenomena

appear (Case 3). It would be difficult to harmonize the conception of a single pacemaker with regularity of auricular beats associated with ventricular bigeminy (Case 1; also certain records in Case 2).

Case 2 is peculiarly important. The records indicate that, not only was there complete block from the ventricular to the auricular pacemaker (retrograde block), but that there was impairment of conductivity in the other direction as well. Not only was the auricular pacemaker guarded from the ventricular center but in addition the ventricular pacemaker was guarded from the auricular center. In most of the records there appears to be complete dissociation between the two pacemakers. Under certain circumstances, however, it appears that the downward block was not quite complete and that occasional impulses from the auricular pacemaker excited the ventricle to contraction. We do not see how the records in this case could be interpreted on the basis of a single pacemaker. It appears to be a case of A-V block (almost but not quite complete) in which the sinus area has been suppressed and another center has become the auricular pacemaker. Or rather, from the viewpoint presented above, it is a case of A-V rhythm in which there is interference to the conduction of impulses from the ventricular pacemaker backward to the auricle, resulting in escape at a secondary center; and in which there is at the same time interference to the conduction of impulses from the auricular pacemaker downward to the ventricle. This impairment of downward conduction, if complete, would remove the case from the category of parasystole; for ventricular responses to impulses from the upper center would be impossible in that event, and parasystole could not develop. Such a case presenting evidence of *two sub-sinus pacemakers* discharging impulses simultaneously is of great importance to the question at issue.

This conception of so-called atrioventricular rhythm as a mechanism which may involve a single pacemaker, or which may involve two pacemakers, the one more or less completely guarded from the other, or (rarely) both guarded from each other, appears to us to be necessitated by comparative study of the cases reported. The fundamental relationship, therefore, between cases of simple A-V rhythm, of so-called reciprocal rhythm and of parasystole is at once apparent; the precise mechanism in a given instance being determined by the degree of retrograde conductivity from the ventricular pacemaker.

SUMMARY

In atrioventricular rhythm the normal auricular pacemaker is inhibited and there is uncovered a secondary center from which impulses activate the ventricle and, in uncompleted cases, the auricle as well. In certain cases, however, impulses from the secondary center are not conducted to the auricle. In such instances auricular escape occurs, the auricular center of highest automaticity becoming the pacemaker for

the auricle. The rhythmicity of such a secondary auricular center is subject to the same influence that may affect other centers of impulse formation. In some cases the retrograde blocking of impulses from the ventricular center is incomplete, and the auricular pacemaker is discharged prematurely by those impulses which reach it just before the completion of its automatic period. Impulses from this pacemaker pass not only to the auricle but also toward the ventricle and produce premature ventricular contractions when not interfered with by refractory tissue. Beating of the ventricle in response to impulses both from the ventricular pacemaker and from the auricular center in such cases constitutes parasystole.

Ten cases were studied, three of which are reported in detail. Reciprocal rhythm as an explanation of the records in these cases is considered but evidence against this interpretation is presented. It appears that cases of simple A-V rhythm, of so-called reciprocal rhythm, and of parasystole are fundamentally related; the precise mechanism in a given instance being determined by the state of retrograde conductivity from the ventricular pacemaker.

These cases occur under circumstances associated with sinus depression and lowered conductivity. Digitalis in some instances appears to be a contributory factor.

REFERENCES

Blumgart, H. L., and Gargill, S. L.: Reciprocal Beating of Heart; Electrocardiographic and Pharmacological Study, Am. Heart J. **5**: 424, 1930.

Blumgart, H. L., and Gargill, S. L.: Mechanism of Transitions from Auriculoventricular Dissociation to S-A Rhythm; Its Relation to the Theory of Parasystole, Am. Heart J. **5**: 437, 1930.

Danielopolu, D., and Proca, G. G.: Recherches sur le rhythme atrioventriculaire chez l'homme, Arch. d. Mal. d. Coeur. **19**: 217, 1926.

Dock, W.: Reciprocal Rhythm; Report of a Case in Which Auricular Tachycardia With Partial A-V Dissociation and Atrioventricular Bradycardia, With Reciprocating Rhythm, Were Present, Arch. Int. Med. **41**: 745, 1928.

Dressler, W.: Zur Frage der Entstehung der Interferenz Dissoziation und der retrograden Fortleitung ventriculäre Extrasystolen, Wien. Arch. f. inn. Med. **19**: 611, 1930.

Drury, A. N.: Paroxysmal Tachycardia of A-V Nodal Origin Exhibiting Retrograde Heart-Block and Reciprocal Rhythm, Heart **11**: 405, 1924.

Jones, T. Duckett, and White, P. D.: Atrioventricular Nodal Rhythm; Report of Two Cases Exhibiting Bigemini. Am. Heart J. **2**: 266, 1927.

Gallavardin, L., and Gravier, L.: Bradycardie nodale permanante, Arch. d. Mal. d. Coeur. **14**: 71, 1921.

Geraudel, E.: Le signe de al contraction auriculaire satellite dans le syndrome d'Adams-Stokes, Arch. d. Mal. d. Coeur. **23**: 18, 1930.

Kaufmann, R., and Rothberger, C. J.: Beiträge zur Entstehungsweise extrasystolischer Allorhythmien I-V, Ztschr. f. d. ges. exper. Med. **5**: 349, 1927; ibid. **7**: 199, 1919; ibid. **9**: 103, 1919; ibid. **11**: 40, 1920; ibid. **29**: 1, 1922.

Mobitz, W.: Zur Frage der atrioventriculären Automatie, Deutsch. Arch. f. klin. Med. **141**: 257, 1923.

Scherf, D.: Reizleitungsstörungen im Bundel, Wein. Arch f. inn. Med. **12**: 237, 1926.

Scherf, D., and Shookhoff, C.: Reizleitungsstörungen im Bündel, Wien. Arch. f. inn. Med. **10**: 97, 1925.

White, P. D.: A Study of Atrioventricular Rhythm Following Auricular Flutter, Arch. Int. Med. **16**: 517, 1915.

White, P. D.: Bigeminal Pulse in Atrioventricular Rhythm, Arch. Int. Med. **28**: 213, 1921.

A STUDY OF GALLOP RHYTHM BY A COMBINATION OF PHONOCARDIOGRAPHIC AND ELECTROCARDIOGRAPHIC METHODS*

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THE application of phonocardiographic methods is destined to render useful service in the study of gallop rhythm. The first records published are not of much clinical interest. The tracings are lacking in precision, and the minute details so useful for the interpretation of the sounds are not in evidence. No doubt these faults are to be attributed to the imperfections in the apparatus employed.

A great advance was made with the introduction of precise photographic methods. By the simultaneous application of sound waves with other cardiac tracings, whether those of the radial or carotid pulse, or the electrocardiogram, a further advance was made.

The simultaneous electrocardiogram enables us to draw most valuable conclusions because of the precision of its waves and by its immediate transmission. The second tracing is indispensable for the correct interpretation of the phonocardiograms.

One has only to consult the researches of Lewis,[14] Groedel,[8, 9] Battaerd,[2] Bull,[3] R. H. Kahn,[11] Weiss and Joachim,[21] Selenin and Vogelson,[19] H. Mond and Oppenheimer[17] and ourselves[15, 16] in order to appreciate the advantages of these simultaneous tracings over the single phonocardiograms.

In our study we have used a simple optic phonocardiograph with electric valves which we ourselves have constructed.[5]

Our apparatus registers the phonogram on the same film as a string galvanometer record. The results and the conclusions which we publish here on gallop rhythm are drawn from tracings made according to this method.

We must insist here upon the fact that gallop rhythm does not always have the same origin. We shall leave out of the discussion all varieties of gallop rhythm not of auricular origin and shall confine our attention to *classical auricular gallop rhythm.*

Typical gallop rhythm is produced by the addition to the two normal sounds of a sound auricular in origin or more exactly auriculoventricular. This sound is considered as the result of the shock of the auricular blood wave on a hypotonic ventricle. Almost all authors agree to this explanation of the rhythm which we are about to discuss. Gallop rhythm as such is not of sudden origin. At the beginning it is often indistinct, and the term gallop rhythm cannot be correctly applied at

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this moment. Afterwards this indistinct gallop may disappear altogether or may develop into a real triple rhythm. We shall see that these modifications of the heart sounds which precede the appearance of gallop rhythm are due to auricular phenomena.

For this reason we shall deal not only with well-developed cases of gallop rhythm but also with the indistinct forms referred to above. We shall extend our discussion to several cases of Stokes-Adams disease with their auricular sounds and to other still rarer affections where an auricular sound is perceptible.

Our group of tracings will thus deal with all added *sounds* (not murmurs) of auricular origin including those which do not necessarily constitute cases of gallop rhythm (23 cases of gallop rhythm in 33 observations).

The observations can be classified as follows:

20 cases of hypertension,
5 cases of hypotension,

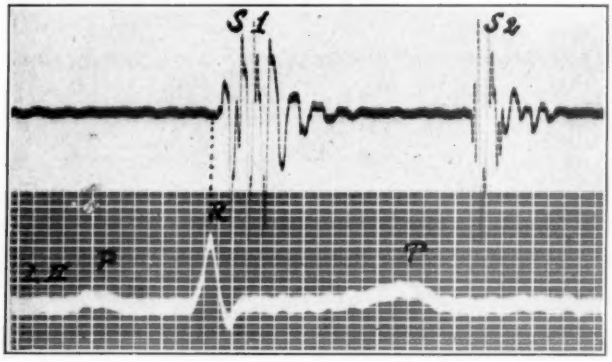

Fig. 1.—Phonogram and electrocardiogram taken simultaneously on a normal subject. The first sound (S_1) begins at the crest of the wave R. The second sound (S_2) appears 0.03 sec. after the end of the wave T. Timing = 1/50 sec.

3 cases of Stokes-Adams disease,
2 cases of extrasystolic arrhythmia,
2 cases of mitral disease,
1 case of congenital heart disease.

In all the cases the auricular origin of the added sound is shown by the presence of the P-wave of the electrocardiogram.

Before undertaking the study of pathological tracings a few remarks should be made upon the chronological relations of the phonogram and the electrocardiogram under normal conditions. A normal tracing is shown in Fig. 1.

The first heart sound begins at the crest of the R-wave of the electrocardiogram and never before it.* It can, however, appear after the crest

*Bridgman[1] and Groedel[10] describe a "normal presystolic sound" which we also have found in some cases, but it is auricular in origin.

of the R-wave in certain cases. It is important to bear in mind this indication in reading the tracings of gallop rhythm which follow. Accordingly no oscillation of the phonogram situated before the R-wave can belong to the first ventricular sound. We attribute the existence of such oscillations in all our observations to the effect of the auricular contraction.

GALLOP RHYTHM IN HYPERTENSION

The observations which follow illustrate the three principal forms of gallop rhythm which one encounters. They correspond at the same time to three different degrees of gravity of the affection. We shall see further on that these forms are the most common. There are others however, which do not fit exactly in this somewhat rough presentation.

CASE 1.—Male sixty-four years old, arterial tension, 210/140 mm. of Hg. Albuminuria; complaining for some weeks of dyspnea and tachycardia, with violent pains in the head. Blood urea, 68 mg. Auscultation of the heart reveals the first heart sound dull and prolonged in the midcardiac area. The second sound especially accentuated. No murmur at the different areas.

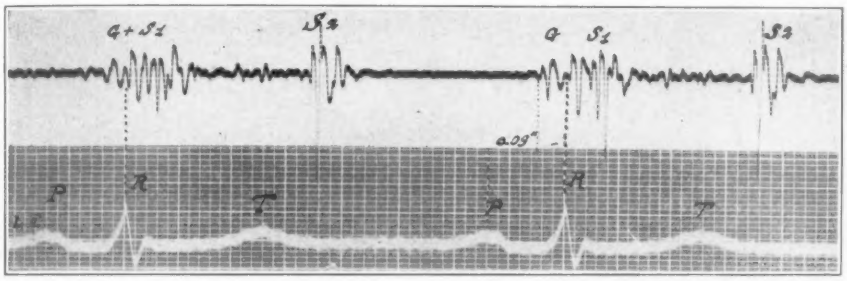

Fig. 2.—Hypertension and albuminuria, slight decompensation. Phonocardiogram and EKG. Male, sixty-four years old. First sound prolonged in the midcardiac area by a short auricular sound (G) jointed to the first sound (S_1). Second sound (S_2) accentuated. Space P-G = 0.09 sec. Immediate and subsequent prognosis good. G disappeared after a short period with remarkable clinical amelioration.

On considering the phonocardiogram (Fig. 2) we notice that the first sound is longer than a normal heart sound. It lasts 0.15 sec. instead of the normal 0.10 sec. The electrocardiogram taken simultaneously furnishes the explanation. It is obvious in fact that two important oscillations precede the R-wave. Their auricular origin cannot be questioned, when we consider the position and the presence of the preceding P-wave.

The case under discussion is not exceptional. It is commonly met in cases of hypertension at the beginning of decompensation. The modification in the auscultatory signs is due to the addition of a slight auricular sound intimately connected with the first ventricular sound. On account of this special chronology the addition of the sound does not give rise to gallop rhythm. It produces a presystolic prolongation of the first sound which should be considered as precursor of gallop rhythm.

CASE 2.—Deals also with a case of Bright's disease. Male, forty-nine years old. In this case, cardiac decompensation is more advanced than in the preceding one.

Effort tachycardia, dyspnea, edema of the feet at the end of the day, albuminuria. Blood urea 68 mg. Arterial tension 205/150 mm. Auscultation at the same time as the taking of the tracing reveals the presence of gallop rhythm produced by the addition to the two heart sounds of a third sound, dull, presystolic, badly defined. For this reason the two first sounds of the rhythm are not clear.

Fig. 3 (Case 2) shows an important group of oscillations of the phonogram before the R-wave of the EKG. This is explained by the auricular contraction P. The lack of distinctness in the rhythm is due to the

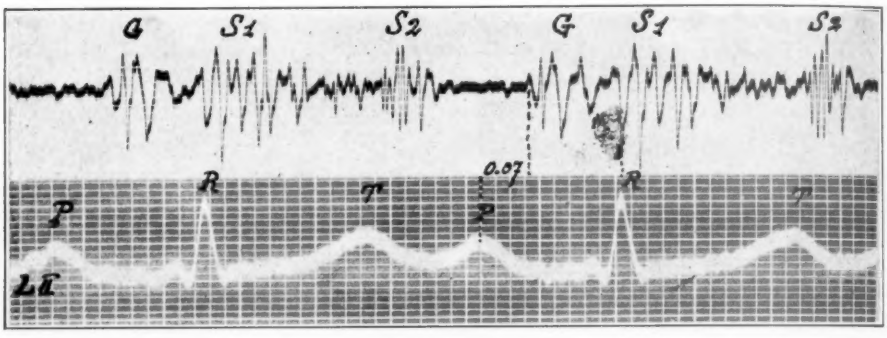

Fig. 3.—Hypertension and albuminuria. Notable decompensation. Male, forty-nine years old. Phonocardiogram and EKG. Indistinct gallop rhythm. Auricular presystolic sound (G) not distinctly separated from the first sound (S_1). The second sound (S_2) is weak. Space P-G = 0.07 sec. Fair clinical prognosis, conditions stationary during the previous six months. Gallop rhythm established during the last two years.

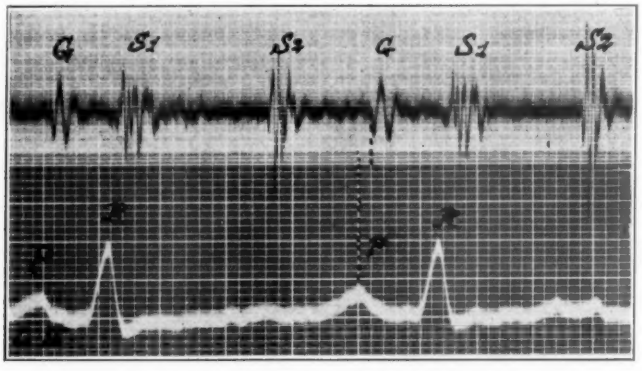

Fig. 4.—Chronic nephritis, terminal cardiac decompensation. Female, forty-seven years old. Phonocardiogram and EKG. Gallop rhythm distinct on auscultation and palpation. Auricular sound (G) presystolic, well separated from the first heart sound (S_1) (silence of 0.08 sec.). Second sound (S_2) accentuated. Space P-G = 0.03 sec. Clinical conditions very bad. The patient died three weeks after the taking of the tracing.

shortness of the silence which separates the two first periods. This lack of distinctness is further accentuated by their dullness.

Case 3.—Bright's disease. Female, forty-seven years old, in a very advanced stage of decompensation. Obliged to remain in bed during the past months, with pronounced swelling of the legs. Permanent dyspnea and albuminuria. Blood urea 30 mg. Auscultation reveals a distinct gallop rhythm accompanied by a presystolic shock which could be easily palpated. Arterial tension 210/150 mm.

The tracing (Fig. 4) reveals the existence of a presystolic sound separated from the first sound by a complete silence of 0.06 sec. This is the classical gallop rhythm which can be perceived equally well by palpation and by auscultation, and the significance of which for the prognosis is well known. The patient died shortly after the taking of the tracing. Post-mortem findings by Professor Askanazy revealed sclerosis and atrophy of the kidneys, considerable hypertrophy of the myocardium—ventricular and auricular—with dilatation of the heart chambers, as is usual in these cases.

In decompensated hypertension the distinctness of the gallop rhythm does not always correspond in such a striking fashion with the gravity of the disease, as in the three cases cited. A certain proportion of such patients may possess a well-defined gallop rhythm for years before declining. Fig. 5 deals with an example of such cases: Female, seventy-

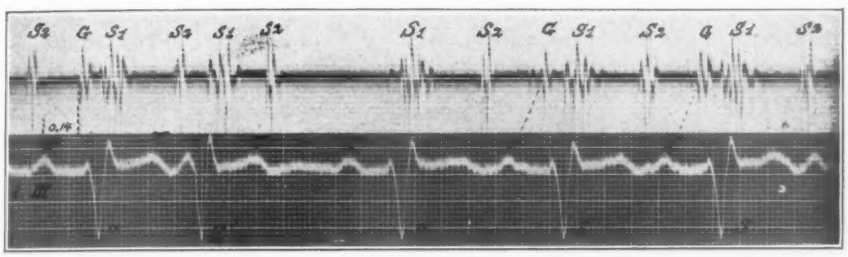

Fig. 5.—Female, seventy-six years old. Hypertension, albuminuria, slight effort dyspnea. Arterial tension 180/130. Phonocardiogram and EKG. Well defined gallop in evidence by auscultation and palpation for the past two years. Auricular sound (G) short and loud, separated from the first heart sound by a silence of 0.14 sec. Extrasystole of septum origin followed by a compensatory pause after which gallop rhythm is absent. The space P-R of the EKG is increased (0.24), a fact which contributes to the distinctness of G (in spite of the length of the space P-G = 0.14 sec.). Second sound is intense (S_2). Clinical status gives no immediate cause for alarm.

six years of age, with gallop rhythm during a period of two years, in whom the clinical conditions became no worse.

(We shall discuss later the different factors which influence the distinctness of gallop rhythm.)

GALLOP RHYTHM IN ARTERIAL HYPOTENSION

Gallop rhythm in hypotension, the clinical picture of which has been so well defined by Dumas,[6] owes its origin in almost every case to the classical mechanism of the auriculoventricular shock. In its category, however, the third heart sound is more frequent than in hypertension and can give rise to triple rhythms which must not be confused with presystolic gallop.

Gallop rhythm of hypotension occurs in primary affections of the myocardium, in hemorrhagic shock, in certain diseases such as leucemia and pernicious anemia, and finally in infectious diseases which affect the heart, such as typhoid fever.

We have never had an opportunity to observe indistinct forms of this

gallop comparable with Case 1, previously cited. We do not doubt, however, the existence of such. In the five cases which we have followed, the rhythm is always well defined and in general more distinct than that of hypertension gallop. The tracings of Fig. 6 relate to a patient forty-

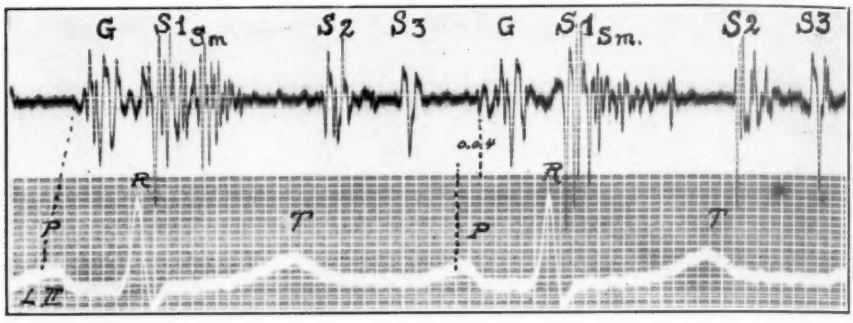

Fig. 6.—Pernicious anemia. Male, forty-nine years old. Hb. 40 per cent, red blood cells 1,225,000. Arterial tension 90/60 mm. Four-time rhythm at the apex. Presystolic sound (G) intense and of high tone, clearly separated from the first sound (S_1). Slight systolic inorganic murmur (Sm). Second sound S_2, third sound S_3. Space P-R = 0.18 sec. Space P-G = 0.04 sec. Serious anemia of grave clinical import. Subsequently cured by liver therapy. Disappearance of G and of S_3.

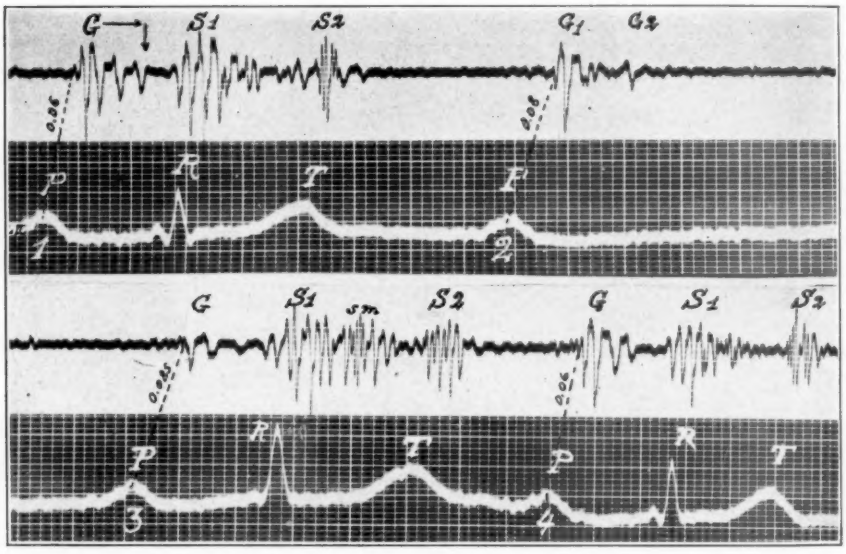

Fig. 7.—Auriculoventricular block produced in a case of hypertension by compression of the carotid (the same patient as in Fig. 3). Phonocardiogram and EKG (owing to its length the tracing is divided into two parts which should be read in succession). The isolated auricular systole (No. 2) gives rise to a double sound G_1 and G_2. The auricular contraction No. 1 produces the sound G which is single, but its total length equals that of the two sounds G_1 and G_2 combined. At the end of the long diastolic pause the sound G is weakened and modified (No. 3). Space P-G No. 1 = 0.06, No. 2 = 0.08, No. 3 = 0.085, No. 4 = 0.06 sec.

nine years old suffering from pernicious anemia. This patient had at the same time gallop rhythm and an exaggerated third heart sound (four-time rhythm of Laubry and Routier). It is useless to insist here on this third heart sound. We shall confine our attention principally to the distinctness and intensity of the added auricular sound.

BLOCK GALLOP IN STOKES-ADAMS DISEASE

In Stokes-Adams disease, auricular sounds are generally imperceptible, but in almost all cases these auricular sounds appear on the tracings. The tracings of Lewis, Groedel, Selenin and Vogelson support this statement. The tracing of Fig. 7 represents the heart-block brought about by the compression of the carotid in the case of hypertension as depicted in Fig. 3. Here the oscillations of phonocardiogram of the isolated auricular systole comprise two crests G_1 and G_2. In fact, in almost all cases the auricular sounds in heart-block are doubled. We ourselves[17] have already published two cases where this doubling was even more striking. W. Reid,[19] Groedel, Selenin and Vogelson have also recorded similar cases. As to why the auricular sound is double in heart-block and single in presystolic gallop, we cannot say. But the fact exists, and our tracing, Fig. 7, illustrates this point.

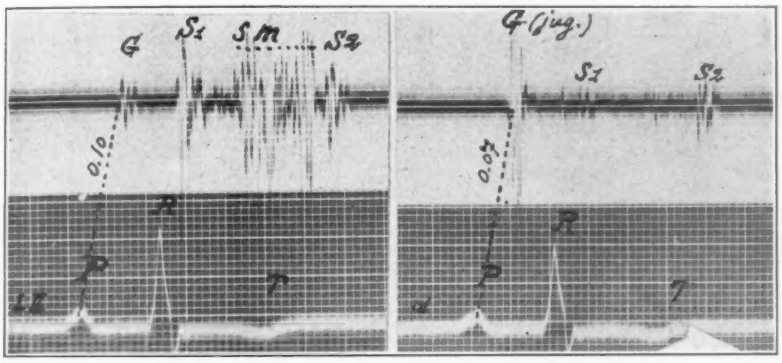

Fig. 8. Fig. 9.

Figs. 8 and 9.—Perforation of the interventricular septum. Absence of cardiac decompensation. X-ray shadow of the heart increased in all its diameters. Fig. 8, to the left, is the record at the aortic area. G is the presystolic sound, S_1 is the first sound, Sm is the systolic murmur, and S_2 the second sound. Space P-R = 0.24 sec. Space P-G = 0.10. On the right, Fig. 9 is a record of events above the left collar bone. G represents the intense presystolic sound, S_1 the feebly transmitted first sound, S_2 the second sound. Space P-G = 0.07 sec.

The wave P (No. 1) preceding the ventricular systole produces a single sound G, while the corresponding sound is doubled in the auricular systole No. 2. It should be noticed that the total length of the double sound is the same as that of the single sound and that reduplication is due simply to the attenuation of intervening oscillations. In one case only of presystolic gallop have we observed a double presystolic G-wave.

AURICULAR SOUNDS IN EXTRASYSTOLIC ARRHYTHMIA

In the case of two normal subjects exhibiting ventricular extrasystoles we have observed on the tracings acoustic waves corresponding to a P-wave coming after the ventricular extrasystole. The only interest attached to these cases is the consideration of the space P-G with which we shall deal later on.

GALLOP RHYTHM AND CONGENITAL DISEASE OF THE HEART

This paragraph deals with an isolated case, that of a young girl twenty years old with a perforation of the ventricular septum, but showing no sign of cardiac decompensation. Auscultation revealed the presence of the usual loud systolic murmur in such a cardiac lesion. In addition, over the whole precardiac region one heard a loud presystolic sound well separated from the systolic sound with its maximum intensity in the aortic area. This sound was also perceptible with extraordinary intensity above the left collar bone. The added sound in this case interests us only from the point of view of auricular etiology, and it cannot be included in a clinical survey of gallop rhythm. Figs. 8 and 9 show the record of this presystolic sound in the aortic area and in the jugular region. Its auricular origin cannot be doubted in view of its relationships with the P-wave. It should be noticed that the space between P and G is 0.03 sec. shorter in the jugular than in the aortic area.

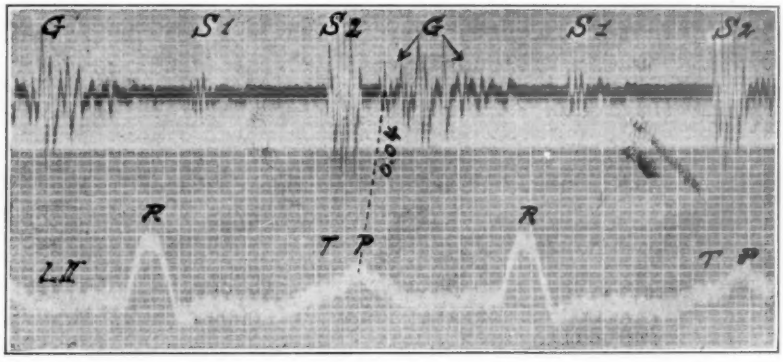

Fig. 10.—Hypertension, nephritis, uremia. Acquired syphilis at the age of twenty-four years. Male, forty-two years, Wassermann positive. Phonocardiogram mid-cardiac and EKG. Diastolic gallop rhythm. Space P-R = 0.30. Added protodiastolic sound G. Dull first heart sound S_1, accentuated second sound S_2. Space P-G = 0.04. Clinical conditions very serious. Patient died eight days after the taking of tracing.

MITRAL STENOSIS AND GALLOP RHYTHM

The anatomical nature of mitral stenosis seems to exclude the production of gallop rhythm. It is difficult to see how the auricular blood wave could give rise to a murmur and a sound at the same time. Several observations, however, among which we must mention the one recorded by Conner, seem to throw doubt on this idea. We ourselves have on two occasions observed an intense additional sound in mitral stenosis. The two cases were very different. In the one case the added sound was certainly due to a third heart sound. In the other case, the added sound was perceptible only in the tricuspid area, while at the apex there was a feeble presystolic murmur. In this latter case we are probably in the presence of gallop rhythm of right ventricular origin. This view is supported by the enormous hypertrophy of the right ventricle.

We cannot discuss with much detail the cases of diastolic gallop caused

by prolongation of the P-R interval, since we have only two tracings at our disposal.

Fig. 10 is an example of diastolic gallop. The auricular sound G is nearer the second sound than the first on account of the prolongation of the conduction time and of the shortness of the space P-G which lasts only 0.04 sec.

The different tracings of gallop rhythm discussed hitherto present certain differences. These differences concern principally the distinctness and the quality of the rhythm which in their turn depend on the intensity and the acoustic qualities of the additional auricular sound. At first sight no general clinical conclusion can be drawn from them. On the other hand the chronological study of the relationships of the wave P with the sound G seems to us to be of great importance in prognosis.

DISTINCTNESS OF GALLOP RHYTHM

The distinctness depends on the intensity of the added sound and the silent space which separates it from the first sound. This space itself is determined by several important factors:

(a) The duration of the sound G. If the sound G is short, it is more likely to be separated from the first sound (cf. Fig. 5).

(b) P-R interval. The prolongation of conduction time throws back into the diastole the sound G, which becomes quite distinct from the first sound, even though it be weak.

(c) P-G interval. As we shall see later on, this interval varies considerably. The longer it is, the nearer the sound G approaches the first sound, and the more indistinct it becomes.

(d) R-S_1 interval. In a few cases, the first heart sound begins several hundredths of a second after the R-wave, which fact separates it more clearly from sound G. Differences in the interval R-S_1 depend also on the area at which the registration is made.

One should be cautious in drawing clinical conclusions from the distinctness of the rhythm, since this depends upon different factors. In diastolic gallop rhythms, Gallavardin[7] has already drawn attention to variations of the interval R-S_1 which are susceptible of modifying this rhythm.

One can, however, conclude that a gallop rhythm whose first two sounds are clearly separated, and where the P-R interval shows no prolongation, is almost always of bad prognosis (cf. further P-G interval).

INTENSITY OF ADDED SOUND G

This varies with the auscultation areas and with the respiration phases in certain cases. In general, the gallop rhythm of hypotension is more intense than that of hypertension.

In one case of a patient with hypertension but whose clinical condition was not serious, the inhalation of amyl nitrite doubled the in-

tensity of the sound G, without notably increasing the heart rate. In the same case pressure exercised on the carotid caused the sound G to disappear almost entirely, while the heart rate dropped only from 78 to 74.

In two cases of auriculoventricular block the auricular sounds were more intense when they occurred at the end of diastole. While in the case of the induced block of Fig. 7, the sound G is sensibly diminished at the end of the long diastolic pause. In another similar case after a block temporarily induced we noticed on the resumption of normal rhythm a considerable weakening of the sound G during a period covering more than thirty systoles.

Ventricular extrasystoles altering the regularity of the rhythm also change momentarily the intensity of the auricular sounds which follow the compensatory pause. In many cases the gallop disappears after an extrasystole, but in one case it was reinforced.

One cannot therefore draw any conclusion as to the prognosis from the intensity of the additional sound.

TONE OF THE ADDED SOUND

The tone differs according to the case. In hypertension it varies between 25 and 50 double vibrations per second. In our five observations of hypotension it oscillates between 40 and 58. In this latter case therefore, it is higher and this fact would explain the distinctness of gallop rhythm in the cases of hypotension.

The G sounds of tone below 30 vibrations are difficult to perceive by auscultation, but they are often perceived on palpation.

DURATION OF THE ADDED SOUND

This varies from 0.04 sec. to 0.15 sec. A long G sound is generally intense, but the contrary is also sometimes observed. The duration of the G sound is no indication of the seriousness of the case.

We have not noticed any relationship between the form of G and that of P.

P-G INTERVAL, OR TIME BETWEEN THE P-WAVE AND THE AURICULAR SOUND

This time is measured from the middle of the P-wave to the beginning of the sound G. Figures taken on our tracings lead us to formulate two important laws.

First law: The duration of the P-G interval is an index of the seriousness of the affection.

This law applies to all the cases of auricular sounds which we have presented here, independent of their variety, whether the nature of the gallop be presystolic or diastolic; whether it occur in cases of block, mitral stenosis, congenital affections, etc. The duration of the P-G interval varies from —0.02 to 0.14 sec. according to the case and is completely independent of the intensity of the sound G.

The maximum variation of the P-G interval is 0.01 sec. according to the area at which the tracing is made. Rhythmic troubles, such as extrasystoles, induced block, bradycardia or tachycardia, never modify it by more than 0.02 sec.

Whenever the interval P-G is less than 0.05 sec., prognosis is very bad. When it is greater than 0.05 sec., cardiac decompensation is less accentuated and a longer survival is probable. The observations presented in

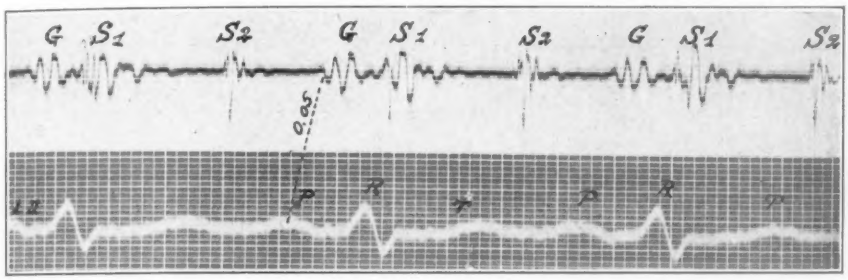

Fig. 11.—Myocarditis with rapid evolution. Tracings recorded January 6. P-G interval 0.05 sec., arterial tension 105/70. EKG, low voltage in three leads.

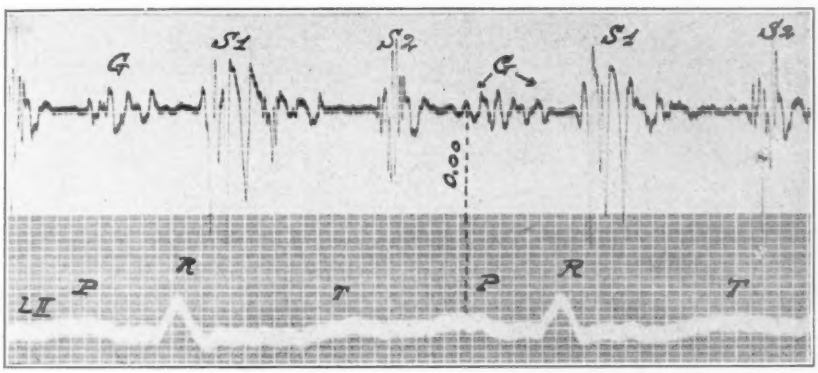

Fig. 12.—The same patient as in Fig. 11. Clinical condition much worse. Tracings made January 12. Gallop rhythm distinct as before. P-G interval = 0.00.

this communication include one exception only to this law. To illustrate our first law, we shall now give a brief summary of our cases:

P-G interval less than 0.05 sec. Twelve very serious cases, in ten of which the patients died within two months, and two survived. Of the survivals one was a case of pernicious anemia treated and cured by liver extract, the other case was one of myocarditis whose condition improved.

P-G interval greater than 0.05 sec. Twenty cases in which cardiac decompensation was not far advanced and in which the clinical condition gave reason to hope for a reasonably long survival. In this group is included the single exception to which we have above referred—one case of serious myocarditis.

Second law: The P-G interval varies in proportion to the amelioration or the aggravation of the case during its evolution.

For example the condition of a patient with gallop rhythm whose P-G interval measures 0.06 sec., might become worse and the interval P-G then becomes less, or on the other hand the condition of the patient might improve and the P-G interval then becomes greater than 0.06 sec. In certain rare cases a patient whose clinical condition is very serious and whose P-G interval measures 0.03 sec. might have a temporary improvement on a suitable medical treatment, and in that case the interval P-G would increase to 0.05 sec. or more.

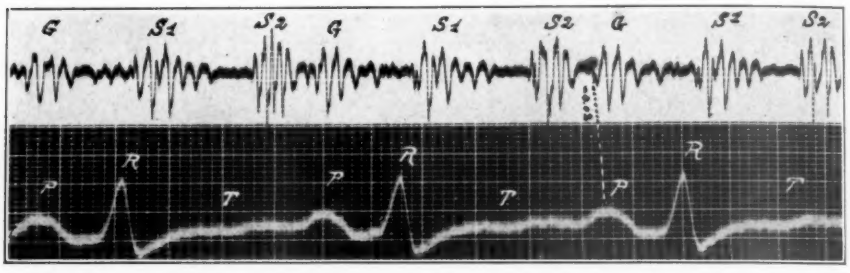

Fig. 13.—Myocarditis. Male, forty-eight years old, alcoholic, Wassermann negative. Blood urea 0.06 per cent. Albuminuria 0.05 per cent. X-ray examination showed the heart sensibly increased in size especially the left ventricle. Tracing taken June 8, 1931, during a serious attack of decompensation. Diastolic gallop rhythm. P-G interval 0.02 sec. decompensation.

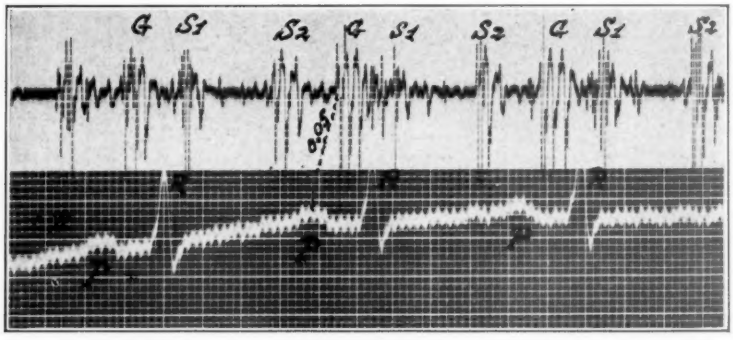

Fig. 14.—Same patient as in Fig. 13. Tracings taken July 13. Considerable clinical amelioration in progress. Gallop rhythm still distinct. P-G interval 0.05 sec.

We shall cite two typical examples of the variations in the length of the P-G interval during the evolution of the disease.

The first example is that of a man forty-four years old, with fibrosis of the myocardium, whose decline was extraordinarily rapid. Hardly four weeks elapsed between the appearance of the first serious symptoms of cardiac decompensation and death. He had rheumatic fever at the age of fourteen, diphtheria at twenty-seven years, no history of syphilis. The first signs of cardiac deficiency appeared in November, 1930. An attack of angina pectoris occurred at the end of December. He had an arterial tension of 170/90. In the beginning of January, 1931, he had acute pain across the chest with intense dyspnea. Auscultation revealed a distinct gallop rhythm. The patient became worse and died January 16. Post-mortem findings by Prof. Askanazy showed the weight of the heart to be 620 gm. There were traces of a previous pericarditis; the valves were intact, and the muscle was much hypertrophied. In the substance of the myocardium appeared large white patches of dif-

fuse myocarditis. The coronary arteries were patent, with slight sclerosis especially at their aortic origin. The four cavities were dilated.

The phonogram tracings taken ten and four days before death are shown in Figs. 11 and 12 respectively. In six days the P-G interval decreased from 0.05 sec. to 0.

The other case deals with a man forty-eight years old, suffering from myocarditis. On entering the hospital his cardiac symptoms were so serious that a fatal issue was supposed to be a question of hours. Diastolic gallop rhythm, easily palpated and clearly audible, was in evidence (Fig. 13). Arterial tension 165/150 mm.

Under the influence of venesection, ouabian parenterally, and subsequently the use of insulin and glucose, the patient gradually improved and after five weeks he could walk a little. It was at this time that the second tracing (Fig. 14) was taken.

On the tracing taken June 8, the P-G interval is negative and measures —0.02 sec. The very early appearance of gallop in relationship to P explains the diastolic appreciation of this gallop, in spite of the fact that the P-R interval is only 0.19 sec. in duration. The second tracing shows the gallop rhythm still distinct, but the P-G interval measures then 0.05 sec. This figure, although still indicating reserve in prognosis, reflects the extraordinary amelioration which took place during five weeks.

CONCLUSIONS AS TO THE MECHANISM OF GALLOP RHYTHM

The auriculoventricular mechanism is confirmed by the phonograms. The origin of the added sound can no longer be doubted. The sound is perceptible only in the ventricular area and not in the auricular. Its origin is not therefore due to the muscular contraction of the auricles. It is generally admitted that the hypotonicity of the failing myocardium causes the ventricle to dilate suddenly and loudly under the influence of the auricular blood wave.

How is one to interpret the variations of the P-G interval? This is not an easy question to answer. The two principal factors in the production of gallop rhythm are the auricular contraction on one hand and the ventricular hypotonicity on the other. It is reasonable to suppose that the modifications in the P-G interval are the result of variations in these two factors during the evolution of the disease.

If the ventricular hypotonicity increases with the gravity of the case, one might suppose that the auricular wave-shock would cause the ventricle to expand more easily and the G sound would be more quickly perceived.

On the other hand, it is possible that the volume of the auricular contraction is greater when cardiac decompensation is far advanced on account of venous stasis. If this possibility be borne in mind, the quick transmission of the auricular G sound can be plausibly accounted for.

Against the argument based on the hypotonicity of the ventricle, one can say that this latter should retard the transmission of the auricular blood wave, and *ipso facto* the sound.

In our opinion more importance should be attached to the increased volume of the auricular blood-wave in advanced decompensation. We do not wish, however, to deny the importance of ventricular hypotonicity in the production of the sound; this fact is no longer questioned.

Our conclusions upon this point are the following:

Muscular hypotonicity of the ventricle is necessary for the production of gallop rhythm. This factor alone, however, is not sufficient to explain all the phenomena of gallop rhythm as indicated in our tracings. Simple auscultation does not reveal these phenomena. From the study of our tracings we are of the opinion that the variations in the P-G interval arise from the variations in the force and volume of the auricular wave, while the hypotonicity regulates the production and the acoustic quality of the sound.

REFERENCES

1. Bridgman, E. W.: Notes on a Normal Presystolic Sound, Arch. Int. Med. **14**: 475, 1914.

2. Battaerd, P. J. T. A.: Graphic Researches on the Acoustic Phenomena of the Heart in Normal and Pathologic Conditions, Heart **6**: 121, 1914-1915.

3. Bull, L.: On the Simultaneous Record of the Phono- and Electrocardiogram, Quart. J. Exper. Physiol. **4**: 289, 1911.

4. Conner, L. A.: Occurrence of Unusual Form of Gallop Rhythm, Am. Heart J. **2**: 514, 1927.

5. Duchosal, P.: Note sur l'enregistrement graphique des bruits du coeur à propos d'un nouveau dispositif spécialement adapté à l'inscription simultanée du phonogramme et de l'électrocardiogramme, Arch. d. mal. du coeur **22**: 797, 1929.

6. Dumas, A.: Le galop d'hypotension, J. Med. Lyon **9**: 543, 1928.

7. Gallavardin, L.: Pathogénie due galop diastolique, Arch. d. mal. du coeur **9**: 410, 1920.

8. Groedel, F. M.: Kann die graphische Darstellung der Herztöne die Diagnose fördern? Verhandl. d. deutsch. Gesellsch. f. inn. Med. Kong. **41**: 372, 1929.

9. Idem: Die diagnostiche Bedeutung der graphischen Darstellung der Herztöne. Pathologie und Therapie der Zirkulationsstörungen. VI. Fortbildungslehrgang in Bad-Nauheim. Leipzig, 1929, Georg Thieme.

10. Holt, E: Gallop Rhythm, Am. Heart J. **2**: 453, 1927.

11. Kahn, R. H.: Die Lage der Herztöne im Elektrokardiogramm. Pflüger's Arch. f. d. ges. Physiol. **129**: 291, 1909.

12. Laubry et Pezzi: Les rythmes de galop. Bibliothèque des grands syndromes. Paris, 1926, Gaston Doin.

13. Laubry et Routier: Bruit de galop et rythme à quatre temps. Bull. et mem. Soc. méd. hôp. de. Paris **49**: 1281, 1925.

14. Lewis, T.: The Time Relations of Heart Sounds and Murmurs With Special Reference to the Acoustic Signs in Mitral Stenosis, Heart **4**: 241, 1913.

15. Mozer et Duchosal: Etude électrophonocardiographique du rythme de galop. Arch. d. Mal. du coeur **2**: 65, 1930.

16. Mozer et Duchosal: Le galop du block dans la maladie de Stokes-Adams. Arch. d. Mal. du coeur **4**: 247, 1930.

17. Mond, H., and Oppenheimer, E. T.: Gallop Rhythm in Hypertension, Arch. Int. Med. **43**: 166, 1929.

18. Reid, W. B.: The Auricular Heart-Sounds, J. A. M. A. **76**: 928, 1921.

19. Selenin und Vogelson: Das Phonogramm bei Vorhofflimmern. Ztschr. f. Kreislaufforsch. **7**: 177, 1929.

20. Schütz, E.: Untersuchungen über Herztöne. Ztschr. f. Biol **89**: 353, 1929.

21. Weiss, O., und Joachim, G.: Registrierungen von Herztönen und Herzgeräuschen mittels des Phonoskops und ihre Beziehungen zum EKG. Ztschr. f. klin. Med. **73**: 240, 1911.

LOCALIZATION OF EXPERIMENTAL VENTRICULAR MYOCARDIAL LESIONS BY THE ELECTROCARDIOGRAM

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EFFORTS to localize ventricular myocardial lesions by means of the electrocardiogram were given impetus by the observations of Herrick[1] and later of Pardee[2] on the electrocardiographic changes following proven coronary thrombosis in man. Previously, Smith[3] had described characteristic alterations in the T-wave and R-T segment after ligation of branches of the coronary arteries in dogs. Parkinson and Bedford,[4] in an admirable paper, described and classified the forms of the R-T segment deviations and T-wave changes in myocardial infarction. They found that the R-T deviation was best seen in either Lead I or III, an R-T elevation in Lead I being associated with an S-T depression in Lead III, and vice versa. They classified all curves which possessed the former features (i. e., R-T elevation in Lead I and S-T depression in Lead III) as T_1 type, and those exhibiting the latter (i. e., R-T elevation in Lead III and S-T depression in Lead I) as T_3 type. They found that some of their tracings showed an R-T deviation in a single lead, either I or III, without significant changes in the other two, or in combined Leads I and II or II and III with no alteration of the remaining lead. However, they considered such findings sufficient to warrant the inclusion of these cases in the above classification. They also pointed out that when the R-T deviation was considerable the T-wave, strictly speaking, was not evident; such curves approximated to the monophasic rather than the diphasic type. Definite T-waves became apparent before the R-T segment completely returned to the isoelectric plane, in which case the direction of the apex of T was constantly opposed to the direction of deviation of the R-T segment. Parkinson and Bedford concluded that "all available evidence points to the fact that it is occlusion of the left coronary artery or its branches which produces characteristic T-wave changes," and agreed with Smith[5] that the relation of the infarct to the apex was the important factor in determining modification of the electrocardiogram.

Barnes and Whitten,[6] observing the exact site of infarction at necropsy in a series of cases in which a coronary T-wave or alteration in the R-T interval had occurred, attempted to correlate the site of infarction, the blood supply, as from the right or left coronary artery, and the R-T and T-wave deviations, as classified by Parkinson and Bedford.

Recently, Barnes and Mann,[7] in a preliminary report, have stated that ligation of branches of the right and left coronary arteries in dogs

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resulted in changes of the RS-T segment closely similar to those produced by occlusion of the corresponding branches in man.

In this investigation a study has been made of the R-T segment and T-wave alerations following the production of definitely localized myocardial lesions, the localization of which has been related to the electrocardiographic classification of Parkinson and Bedford.

METHOD

An electric cautery was applied to the heart in order to produce a lesion simulating that of myocardial infarction. To facilitate the interpretation of results the ventricular wall was arbitrarily divided into the following eight regions: left apex anterior, left base anterior, left apex posterior, left base posterior, right apex anterior, right base anterior, right apex posterior and right base posterior. Thirty-four successful experiments were performed on cats under sodium amytal anesthesia (75 mg. for an adult cat injected intraperitoneally). Needle electrodes were placed under the skin and tied, the control electrocardiogram being taken after this step. Artificial respiration was then established, the chest opened, and the whole heart exposed by slitting the pericardial sac. A second tracing was recorded, the time noted and the cautery applied to one of the above regions until a burn of about ½ cm. in diameter was produced. The depth of the burned area was extended as far as possible without penetrating the ventricular cavity. If this precaution were taken very little bleeding ensued. The time was noted and a third electrocardiogram recorded. If it showed no change from the normal, the boundaries of the cauterized area were slightly extended. Thereafter, tracings were taken at frequent intervals, and at the completion of the experiment the heart was removed, examined, and preserved in alcohol.

RESULTS

In analyzing the results, the classification of Parkinson and Bedford of T_1 and T_3 types has been adopted as a basis. When individual cases do not conform, the differences are stated. One can either describe the electrocardiographic changes produced by a lesion in a particular area or note the areas from which curves of a definite type were obtained. The former method seems preferable, for by this means all the information given by the latter is included and variations from the basic type are more easily presented. All curves which could be classified definitely were of a monophasic type. In a majority of the experiments the electrocardiographic changes which followed cauterization were only transient and a return to normal ensued despite the continued existence of the lesion. The significance of this will be discussed later. In some instances there was present between the monophasic type of curve and the return to normal, a transitional stage in which a diphasic curve was seen, with the terminal deflection resembling the coronary T-wave.

Left Apex Anterior (Figs. 1 *B*, 2 *A*, 7 *A*).—Eight successful experiments were performed, in six of which typical T_1 curves were obtained. In two of these (Cats 3, 26) Lead III presented a low take-off of the R-T interval,* while in the other four (Cats 1, 13, 20, 30) it showed no

*R-T interval will be used throughout for both the R-T and S-T interval.

TABLE I

CLASSIFICATION OF ELECTROCARDIOGRAMS ACCORDING TO TYPES

SITE OF LESION	CAT NO.	TYPE		DEGREE OF CHANGE	REMARKS
Left Apex Anterior	1*	T_1		definite	
	3	T_1		definite	
	4	?			R-T elevation in Leads I, II, III of equal magnitude
	13	T_1		definite	changes not marked
	20	T_1		definite	
	26	T_1		definite	
	27		T_3	definite	
	30	T_1		definite	
Left Base Anterior	5	?			R-T depression in Leads II and III
	10	T_1		definite	
	21	T_1		slight	
	24	?			R-T depression in Leads I and II
	29	T_1		definite	
Left Apex Posterior	6		T_3	definite	
	22		T_3	definite	
	31		T_3	definite	
	34		T_3	definite	
	1*		T_3	definite	
Left Base Posterior	7		T_3	definite	
	9		T_3		R-T elevation in the 3 leads most marked in Lead III
	23		T_3	definite	
	33		T_3	definite	R-T elevation in the 3 leads most marked in Lead III
	35		T_3	definite	
Right Apex Anterior	12		T_3	definite	
	14		T_3	definite	changes not marked
	32		T_3	definite	changes not marked
Right Base Anterior	11				no change in any of the leads
	17		?		slight depression in Lead II
	39				no change in any of the leads
Right Apex Posterior	16		T_3	definite	
	36		T_3	definite	changes not marked
	40		T_3	definite	
Right Base Posterior	15		T_3	definite	changes not marked
	37		T_3	slight	
	38		T_3	definite	

*In this experiment, a lesion was produced first at the left apex anterior. When the changes induced had disappeared, the left apex posterior was cauterized.

change from normal. In one instance (Cat 4) a monophasic curve of about equal magnitude was produced in the three leads. Cat 27 was an exception to all the other experiments performed at this site in that a typical T_3 tracing was obtained. A later record in this case showed a coronary T-wave.

Left Base Anterior (Fig. 2 *B*).—Five successful experiments were performed, in two of which (Cats 10, 29) the curves obtained were

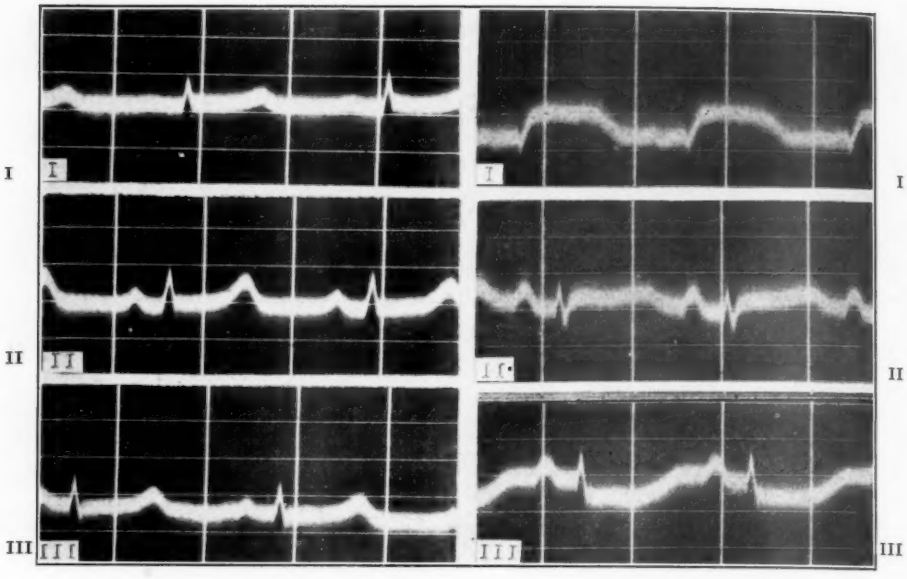

Fig. 1.—*A*. Normal. *B*. Lesion at left apex anterior. T_1 type. Marked R-T elevation in Lead I and depression in Lead III. Time 1/5 sec. 1 cm. = 1 millivolt.

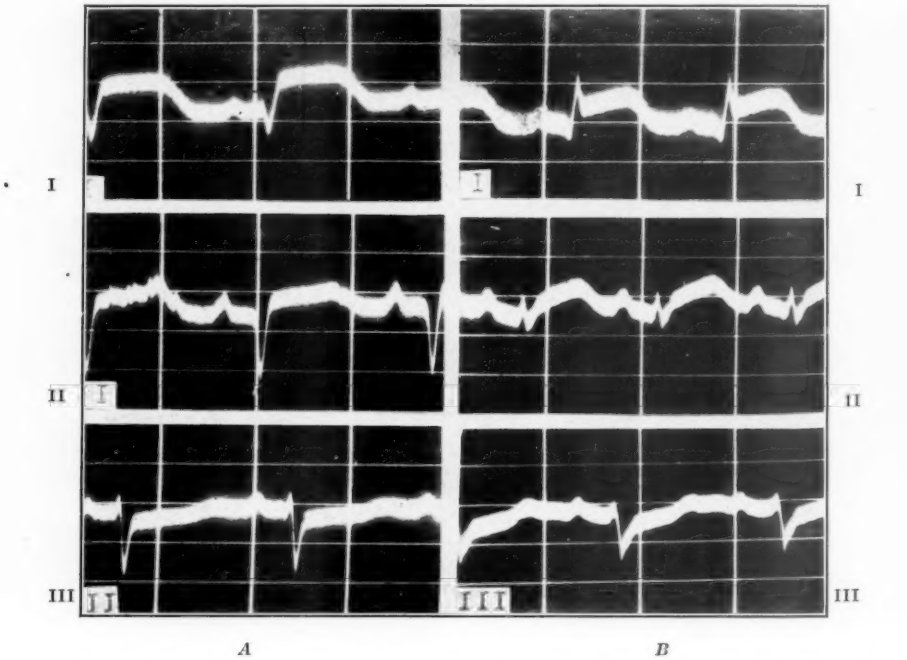

Fig. 2.—*A*. Lesion at left apex anterior. T_1 type. R-T elevation in Lead I and depression in Lead III. *B*. Lesion at left base anterior. T_1 type. R-T elevation in Lead I and depression in Lead III.

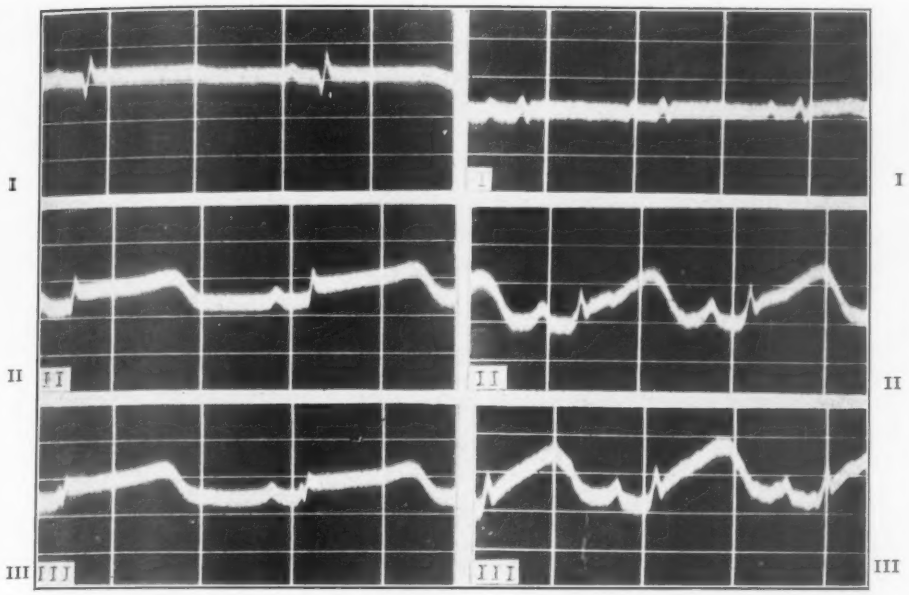

Fig. 3.—*A*. Lesion at left apex posterior. T_3 type. R-T elevation in Lead III and no change in Lead I. *B*. Lesion at left base posterior. T_3 type. R-T elevation in Lead III and no change in Lead I.

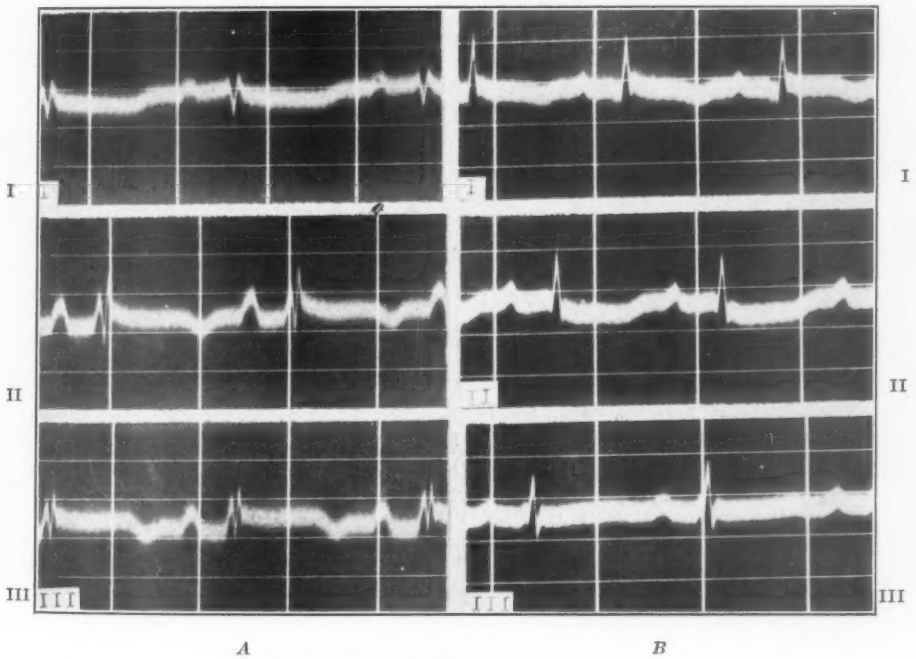

Fig. 4.—*A*. Lesion at right apex anterior. T_3 type. R-T elevation in Lead III and slight depression in Lead I. *B*. Lesion at right base anterior. Type undetermined. Slight R-T depression in Lead II.

markedly of the T_1 type, while in a third (Cat 21) there were similar but less pronounced changes. In Lead III, Cat 29 showed no alteration of the R-T segment, Cat 21 a slight depression and Cat 10 a slight elevation which was almost negligible compared to that in the other leads. Cat 24 presented a slight depression of the R-T interval in Leads I and II, and no change in Lead III. In Cat 5 there was a depression in Leads II and III, while Lead I remained unchanged (Fig. 6 *B*).

Left Apex Posterior (Figs. 3 *A*, 7 *B*).—Four successful experiments (Cats 6, 22, 31, 34) were performed and in every instance a T_3 type of

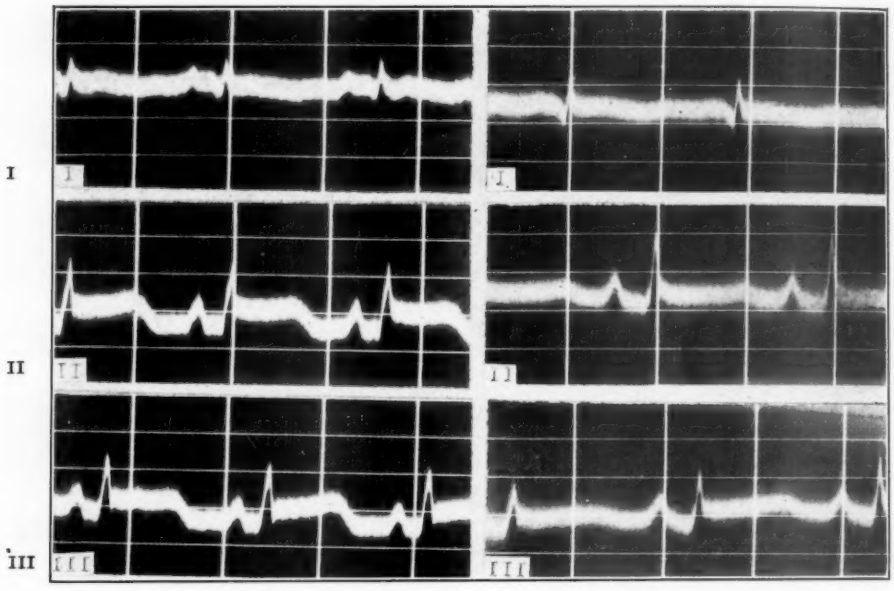

Fig. 5.—*A*. Lesion at right apex posterior. T_3 type. R-T elevation in Lead III and no change in Lead I. *B*. Lesion at right base posterior. T_3 type. R-T elevation in Lead III and no change in Lead I

curve was obtained. No change from the normal was observed in Lead I in any of these.

Left Base Posterior (Fig. 3 *B*).—Five successful experiments were performed, in three of which (Cats 7, 23, 35) typical T_3 curves resulted. Lead I in all of these remained unchanged. Cats 9 and 33 presented an elevation of the R-T interval in the three leads but most marked in Lead III (Fig. 6 *A*).

Right Apex Anterior (Fig. 4 *A*).—Three successful experiments were performed. Cat 12 showed a well marked T_3 type with a slight depression of the R-T interval in Lead I. The other two (Cats 14, 32) presented T_3 types, but the changes produced were much less marked. Lead I in both of these was unaltered.

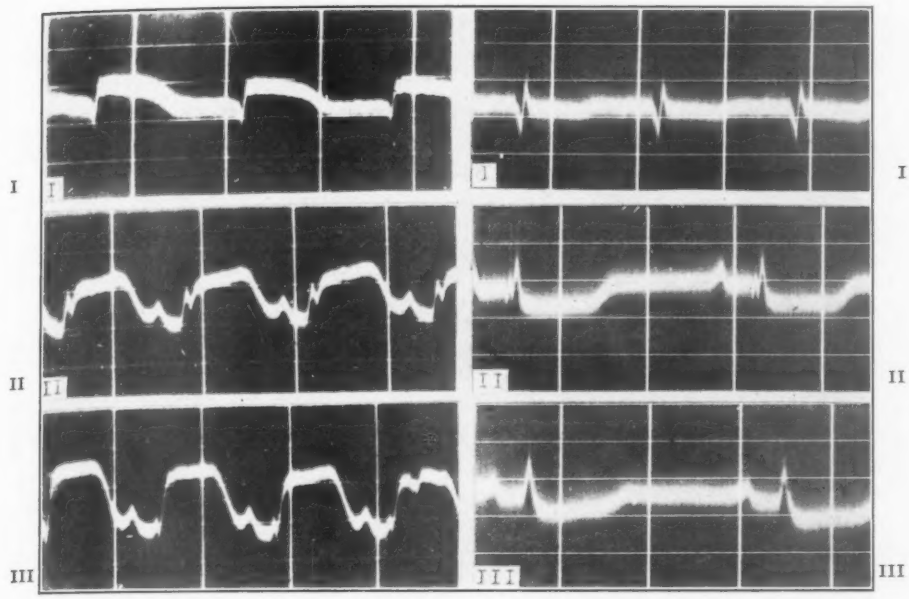

Fig. 6.—Curves presenting unusual characteristics. *A*. Lesion at left base posterior. R-T elevation in all three leads, most marked in Lead III. *B*. Lesion at left base anterior. R-T depression in Leads II and III.

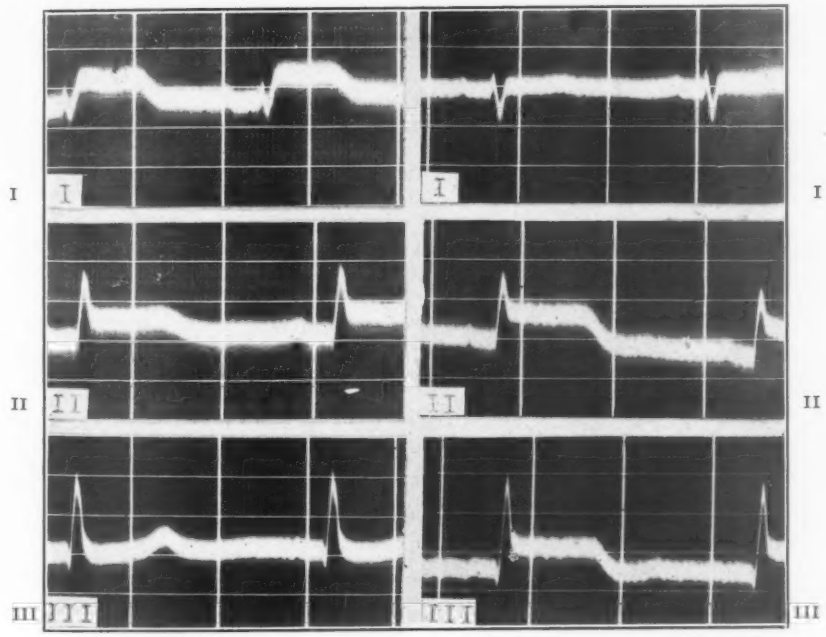

Fig. 7.—*A*. Lesion at left apex anterior. T_1 type. R-T elevation in Lead I and no change in Lead III. *B*. Lesion produced at left apex posterior in the same heart after recovery from *A*. T_3 type. R-T elevation in Lead III and no change in Lead I.

Right Base Anterior (Fig. 4 *B*).—Three successful experiments were performed (Cats 11, 17, 39) none of which showed any marked change in the curves, despite repeated cauterization. However, in one (Cat 17) a slight depression of the R-T interval was observed in Lead II.

Right Apex Posterior (Fig. 5 *A*).—Three successful experiments were performed, in all of which a T_3 type of curve resulted. Two (Cats 16, 40) showed a marked change, while in the other (Cat 36) it was slight but definite. Lead I remained unchanged in two, while in one (Cat 40) it presented a marked depression of the R-T interval.

Right Base Posterior (Fig. 5 *B*).—Three successful experiments were performed (Cats 15, 37, 38) in all of which a T_3 type of curve was produced. Cat 37 showed a slight but definite depression of the R-T segment in Lead I. In none of the curves were the changes as great as had been obtained at the right apex posterior.

DISCUSSION

Previous investigators have employed various methods to produce in animals a condition simulating coronary occlusion with subsequent myocardial infarction in the human being. As early as 1862, Panum[8] attempted to obstruct the coronary arteries by injecting a mixture of oil, wax, tallow and lampblack into the aorta, but his work is only of historical interest, since the results were inconclusive. Porter[9] and later Hamburger, Priest and Bettman[10] injected suspensions of lycopodium spores directly into individual coronary arteries. The latter group of investigators, who performed their work on dogs, stated that the subsequent lodgement of these emboli in capillaries and arterioles more nearly approximated the clinical finding of coronary thrombosis than the ligation of larger branches.

A number of workers, Samuelson,[11] Porter,[9] Miller and Matthews,[12] Kahn,[13] Otto,[14, 15, 16] Smith,[3, 5] Feil and his collaborators,[17] Barnes and Mann[7] and others, have utilized ligation or clamping of coronary arteries to produce the desired lesion. Feil and his coworkers were careful to exclude the coronary vein from the ligature, which limited the ischemia to coronary artery occlusion, a precaution not taken by previous investigators. Feil further increased the existing myocardial ischemia by occluding the inferior vena cava at various periods during the experiment.

Several investigators have attempted to inject various chemicals into the myocardium of the ventricles in order to produce results similar to infarction. Eppinger and Rothberger[18] injected a 5 per cent solution of mercuric chloride, but they soon discontinued it because of fear that the absorption of the poison would cause complications, and furthermore, it was difficult to recognize the injected area after the heart was fixed in formalin. Later, they used a 20 per cent solution of silver nitrate and found it served very well; the region affected was clearly seen

macroscopically and well outlined microscopically. Smith[5] employed mercuric chloride and nitric acid, but because he experienced difficulty in limiting the effects of these caustics to definite areas of cardiac muscle, the method was discontinued. The same criticism holds for the procedure of Otto[16] who injected 95 per cent alcohol into the myocardium.

Heat and cold were applied to various parts of the heart by Eppinger and Rothberger[18] and Smith.[5] They sprayed ethyl chloride on the epicardial surface of the heart, Smith also applying small pledgets of cotton, some of which had been soaked in water of 120° F. and others in ice water. But the objection to these procedures is that only a fleeting effect was produced, and since subsequent histological examination revealed no marked change in the region which had been subjected to the heat or cold, it was likewise difficult to make any definite localization.

The advantage of the method used in this work is that lesions similar in location and other respects can be reproduced in a series of experiments. This does not apply to the procedure of ligating coronary vessels, for the blood supply to the ventricles varies, with the result that tying off the corresponding vessel in different hearts will not necessarily cause infarction of precisely similar regions in each case. With the cauterization method there is no fear of constitutional effects as is present in the case of injection of caustics. The lesion produced is permanent and definitely demarcated from the surrounding tissue, in contradistinction to that resulting from the application of heat and cold which is transitory and difficult to recognize either macroscopically or microscopically.

Samojloff,[19] in his interpretation of direct lead curves obtained after pinching or cutting the apex of the frog's heart, inferred that the effect produced was a manifestation of the injury current. In injured muscle, injured-uninjured lead-offs demonstrate a difference of potential, the injured part being "negative" to the uninjured. Upon stimulation of the uninjured portion, the wave of excitation spreading toward the injured end is expressed electrically as a decremental variation of the already existing demarcation current. When injured-uninjured lead-offs are taken from the heart, the electrogram of each ventricular response is a monophasic type of curve substantially similar to that resulting from excitation of a strip of locally injured muscle.

Attracted by the striking resemblance, most authors have explained the so-called coronary type of R-T segment deviation in the electrocardiogram as an expression of the monophasic action current similar to that demonstrated by leading directly from the injured heart. Variations in the form, amplitude and duration of the waves in the indirect derivation as compared with the direct were related to the method of leading off. Craib[20] among others does not accept this view. He states that "clinical variations in the T-wave are not to be compared with monophasic curves experimentally obtained from exposed and partly

injured hearts directly led off from injured and uninjured regions respectively." He considers that the alterations in the electrocardiogram resulting from local myocardial injury depend upon the failure of the injured region to contribute its normal component to the electrical field.

Aside from the respective merits of the above views, the use of the term "monophasic" in this paper requires further modification. Craib[20] has shown that diphasic curves are obtained from injured muscle, cardiac as well as skeletal, if the tissue is surrounded by a large moist conductor. An initial brief positive deflection precedes the relatively prolonged negative variation. According to the doublet hypothesis, the electrical field in the fluids bathing the tissue is determined by the simultaneous presence of an anode and a kathode at the tissue surface arising from a common electromotive source within the tissues, so oriented that during invasion the anode leads while during retreat the kathode leads. The initial positive deflection, therefore, is held to be due to the arrival of the anode under the uninjured lead-off. It is recognized that smooth monophasic curves are not easy to obtain from the mammalian heart even with direct leads. Drury and Brow[21] concluded that only an approximation could be obtained, and Katz[22] discussed the difficulties and reviewed the literature. However, the variations in question are limited to the initial deflections, and our problem is concerned with the end deflections only. Therefore, despite the conflicting views as to the origin of the changes following injury, we have chosen to use as a descriptive term "monophasic type," with which so many readers are familiar, to designate the R-T segment deviations.

Barnes and Whitten[6] in their investigation endeavored to correlate the artery thrombosed, the area infarcted and the electrocardiographic changes produced. They found in the average normal heart that the left coronary artery supplied "the entire anterior surface of the left ventricle, the adjacent third of the anterior surface of the right ventricle, the apex of both ventricles, all of the interventricular septum at the apex, the anterior two-thirds of the septum above that point, and the left half of the posterior surface of the left ventricle." The remainder of the heart was supplied by the right coronary artery. They studied forty-seven cases and found in twenty-one of these in which the electrocardiograms were of the T_1 type, that the infarction occurred in the anterior and apical portions of the left ventricle in the region supplied as a rule by the left coronary artery. In six cases in which T_3 type had been present the infarction was in the posterior part of the left ventricle in the region usually supplied by the right coronary artery. Four cases showed a change, while under observation, from one type to the other. It was found on autopsy in these that two infarcts were present and that the above rule obtained, i. e., if the older infarct were in the anterior part of the left ventricle T_1 type would be present originally while the more recent infarct in the posterior part of the left ventricle caused a shift to the T_3 type and vice versa. In the only instance

in which multiple lesions were carried out in our experiments (Cat 1) we were able to corroborate this finding. The left apex anterior was cauterized and a typical T_1 tracing was obtained. After a time the electrocardiogram returned to normal and then a lesion was produced at the left apex posterior which caused a typical T_3 curve to appear (Fig. 7 *A* and *B*). In only one of Barnes and Whitten's cases where a T_3 type was obtained was the infarction found to be in the anterior portion of the left ventricle. In four the type of change in the tracings could not be determined while in seven alterations in the conduction system had been induced which obscured the picture. They concluded that "Infarction limited to the anterior portion of the left ventricle, either alone or combined with infarction of the apex, or infarction of the apex alone, produces modification of the R-T segment of type T_1, whereas infarction of the posterior portion of the left ventricle, with or without infarction of the apex, produces modification of the R-T segment of type T_3." They believe that as far as the electrical forces which effect the R-T segment are concerned the left ventricle can be divided into an anterior two-thirds including the apex and a posterior third. Parkinson and Bedford had found that infarction of the right ventricle was rare, a fact which was corroborated by Barnes and Whitten. Bell and Pardee[23] described five cases of their own and seven which Levine[24] had reported and found that the tracings and autopsy results corresponded in the same manner as those of Barnes and Whitten. A case has been described by Bates and Talley[25] and another by Purks[26] in which stab wounds of the chest cut the left anterior descending artery, and in both of these T_1 type of electrocardiogram resulted. Gilchrist and Ritchie[27] in an analysis of their records confirmed the findings of Parkinson and Bedford. However, they were unable to substantiate the views of Barnes and Whitten in a comparison of electrocardiograms and autopsy reports in one case of their own and in cases previously published by other authors.

When one attempts to correlate the R-T deviations with the site of myocardial damage, produced either by coronary occlusion or local injury, the earlier experimental work is inapplicable to the problem in that no electrocardiograms were taken. Likewise, the work of Samojloff[19] and Eppinger and Rothberger[18] can not be considered, as standard leads were not used. On analyzing the earlier work of Smith[3] one finds inconsistency in the type of curve obtained after the ligation of corresponding arteries in a series of dogs. In his later work[5] which included the use of heat and cold, and the injection of nitric acid and mercuric chloride, the results cannot be applied as only Lead II is illustrated and no description of the changes in individual leads is given. Hamburger, Priest and Bettman[10] also obtained inconsistent results. Most of the work of Otto is inapplicable as he used only Lead II or chest leads. In one paper[14] in which standard leads were taken he found that ligation of the second large branch of the left circumflex artery caused

an R-T fusion in Leads I, II and III, or in II and III, while inconstant R-T fusion resulted from the ligation of the left anterior descending branch. He considered that the former supplied the left part of the posterior surface of the left ventricle. However, it is difficult from the description to localize the probable area of damage. He states that ligating the right coronary artery causes S-T depression and fusion. Feil and his coworkers[17] carried out an extensive investigation on dogs which was largely concerned with the problem under discussion. They ligated the left anterior descending artery from which the vein had been separated and found that no characteristic R-T deviation resulted. However, if the blood supply to the heart were further impaired by temporarily ligating the inferior vena cava definite changes appeared. The explanation of Feil that the typical changes are dependent upon a considerable degree of cardiac anoxemia seems to be well founded. It is probable that in the production of our lesions, handling the heart caused general cardiac anoxemia. Feil and his coworkers were unable to substantiate the views of Barnes and Whitten. Although the changes in Lead I showed fair agreement with their thesis, considerable disparity in Leads II and III was present. However, Barnes and Mann,[7] in a later investigation, reported that ligation of the branches of the left coronary artery in the dog resulted in changes in the RS-T segment of the electrocardiogram which are closely similar to those produced in man following obstruction of the anterior descending branch of the left coronary artery, and leading to acute infarction in the anterior and apical portion of the left ventricle. Likewise, the changes of the RS-T segment produced by ligation of branches of the right coronary artery are closely similar to those of occlusion of the right coronary artery in man, and resulting in infarction in the posterior basal portion of the left ventricle.

In all our results a monophasic type of curve was obtained except at the right base anterior. In the great majority of instances the curves could be definitely classified as T_1 or T_3 type. The changes in Lead II resembled those of Lead I in the T_1 type and those of Lead III in the T_3 type. In two instances an elevation of the R-T interval was seen in all leads, but it predominated in Lead III, so that the type could be definitely classified. However, in another the changes appeared to be of equal magnitude in the three leads and it could not be classified. In three experiments, instead of an elevation of the R-T segment the only alteration noted was a depression. The lesions which induced this were at the base of the heart on the anterior surface; two at the left base and one at the right. Of those at the left base one caused a slight depression in Leads I and II, the other in Leads II and III. That at the right base produced a slight depression in Lead II. In some instances in T_1 types the classical picture of a depression in Lead III was obtained, and similarly in Lead I in the T_3 type, but this was not the rule. Parkinson and Bedford found in many of their cases that the typical

changes were not present in all three leads, and did not regard the depression in either Lead I or III a requisite for classification.

When one considers the effect on the electrocardiogram of the location of the lesions, one notes a remarkable degree of constancy. On the anterior surface of the left ventricle, both apex and base, a T_1 type of curve was obtained, except in one instance where cauterization of the apex produced a T_3 type, and in two others where lesions at the base caused a pure depression of the R-T segment in two leads. In one of the latter this depression was present in Leads I and II and in the other in Leads II and III. These curves have not been classified. On the posterior surface of the left ventricle, both apex and base, typical T_3 curves were obtained in every case. It is of some interest to speculate as to the cause of the relative consistency of our results and the inconsistency of those of other workers in their ligation experiments. As has been pointed out, by our method one can produce with considerable degree of accuracy a lesion of approximately the same size, in approximately similar sites in repeated experiments, whereas by ligating a vessel the position and size of the lesion must be modified necessarily by the variations of the blood supply in the individual animals. The site of the lesion produced is of undoubted importance, but the amount of tissue involved has also to be considered. The part of the injured area which at a particular moment is producing the maximal influence on the electrical forces causing the R-T segment might, in a large lesion, vary greatly. When one considers that the left anterior descending branch supplies a variable part of the septum and also sometimes gives branches to the left part of the posterior surface, it is possible that following thrombosis, the portion of the infarct producing the greatest electrical effects might be toward the posterior surface of the heart. This could cause an entirely different picture from that induced by activity towards the anterior surface. It seems unlikely that in all parts of the damaged area an equal degree of change is taking place at the same time.

The changes produced in the right ventricle gave equally definite results. A typical T_3 type of curve was obtained from all sites except the anterior base. On cauterization of the latter site there was no variation from the normal, except in one instance—a slight depression in Lead II. Only at the apex posterior, however, were the changes of the same magnitude as had been found when the left ventricle was cauterized. As noted before, previous observers found greater difficulty in obtaining electrocardiographic effects in lesions of the right ventricle.

Our experimental results substantiate the thesis advanced by Barnes and Whitten from their clinical studies except in one particular, namely that we obtained T_3 type of curves from the left apex posterior. The region cauterized was undoubtedly in the area which they consider to be supplied by the left coronary artery. Whether the discrepancy is due to a different distribution of the blood supply in the cat from the

human, one cannot state at present but studies are in progress to determine the relation of the blood supply to the lesions described. However, it appears most probable, as both Parkinson and Bedford and Barnes and Whitten suggested, that it is the geographical distribution of the lesion rather than any particular blood supply that determines the electrocardiographic changes.

SUMMARY

Electrocardiographic changes were studied in relation to the site of damage in thirty-four cats in which localized ventricular myocardial lesions had been produced by the electric cautery. Monophasic type curves were obtained which were classified as of the T_1 and T_3 types of Parkinson and Bedford. With almost complete consistency lesions in similar sites produced the same type of curve. Lesions on the anterior surface of the left ventricle produced curves of the T_1 type, while those on the posterior surface of the left ventricle, including the apex, yielded the T_3 type. All right ventricular sites, except the base anterior in which only a slight change was induced, gave curves of the T_3 type. At the apex posterior alone were the changes comparable in magnitude with those obtained in the left ventricle. Usually the changes produced were marked in two leads. In some the displacement of the R-T segment was oppositely directed in the remaining lead, while in others no significant deviation was observed in this lead. In a few instances an R-T elevation was present in all three leads but as a rule to a greater extent in one lead. In three experiments, in each of which the lesion was located at the base anterior, depression rather than elevation of the R-T segment occurred.

REFERENCES

1. Herrick, J. B.: J. A. M. A. **72:** 387, 1919.
2. Pardee, H.: Arch. Int Med. **26:** 244, 1920.
3. Smith, F. M.: Arch. Int. Med. **22:** 8, 1918.
4. Parkinson, J., and Bedford, D. E.: Heart **14:** 195, 1927-29.
5. Smith, F. M.: Arch. Int. Med. **25:** 673, 1920.
6. Barnes, A. R., and Whitten, M. B.: Am. Heart J. **5:** 142, 1929.
7. Barnes, A. R., and Mann, F. C.: Proc. Staff Mayo Clin. **6:** 269, 1931.
8. Panum, P.: Virch. Arch. f. path. Anat. **25:** 308, 1862.
9. Porter, W. T.: J. Exper. Med. **1:** 46, 1896.
10. Hamburger, W., Priest, W., and Bettman, R.: Am. J. Med. Sc. **171:** 168, 1926.
11. Samuelson, B.: Ztschr. f. klin. Med. **2:** 12, 1881.
12. Miller, J., and Matthews, S.: Arch. Int. Med. **3:** 476, 1909.
13. Kahn, M. H.: Bost. M. and S. J. **187:** 788, 1922.
14. Otto, H.: Am. Heart J. **4:** 64, 1928-29.
15. Otto, H.: Am. Heart J. **4:** 346, 1928-29.
16. Otto, H.: Arch. Int. Med. **43:** 335, 1929.
17. Feil, H. S., Katz, L. N., Moore, R. A., and Scott, R. W.: Am. Heart J. **6:** 522, 1931.
18. Eppinger, H., and Rothberger, C.: Wien. klin. Wchnschr. **22:** 1091, 1909.
19. Samojloff, A.: Pflüg. Arch. f. d. ges. Physiol. **135:** 417, 1910.
20. Craib, W. H.: The Electrocardiogram, Med. Res. Council Rep. London, 1930.
21. Drury, A. N., and Brow, G. R.: Heart **12:** 321, 1926.
22. Katz, L. N.: Physiol. Reviews **8:** 447, 1928.
23. Bell, A., and Pardee, H.: J. A. M. A. **94:** 1555, 1930.
24. Levine, S. A.: Medicine **8:** 245, 1929.
25. Bates, W., and Talley, J.: Am. Heart J. **5:** 232, 1929.
26. Purks, W.: Am. Heart J. **7:** 101, 1931.
27. Gilchrist, A. R., and Ritchie, W. T.: Quart. Jour. Med. **23:** 273, 1930.

COARCTATION OF THE AORTA (ADULT TYPE). A REPORT OF THREE CASES*

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THREE cases of the adult type of coarctation are reported. Two are new additions to the literature. One has been mentioned previously (Blackford[2]). The latter case is added because of some findings not mentioned in his report.

The history and pathogenesis of coarctation have been so ably reviewed in the literature (Abbott,[1] Blackford[2]) that these features are omitted in this report.

One point which may have a bearing on pathogenesis, particularly for those who still think the condition is of postnatal origin, I wish to mention. Dally[4] in discussing the descent of the diaphragm at birth claims that this descent (contraction) changes the direction of the currents of blood between the auricles and in the ductus arteriosus. He refers to Keith[5] who states: "When the right crus contracts at birth, with the first inspiration, it draws the pulmonary arteries and the fixed margin of the vestibule of the left auricle with it, but the aorta is fixed otherwise and scarcely yields. Hence a decided traction is exercised on the ductus arteriosus, enough I believe to stop the flow of blood from the pulmonary artery to the aorta and turn it into the lung, which at the same time is expanding. . . . . Thus the contraction of the right crus, while helping to expand the lung, also closes the foramen ovale and ductus arteriosus."

That this pull exerted at a distance may be one of the jumble of forces acting on the ductus is merely stated. Its influence on coarctation is of course purely speculative. Those who have seen a case of coarctation at the postmortem table can hardly fail to have received the impression that the real cause of coarctation lies in the anomalous redistribution of the primitive arches which go to make up that area of the definitive arch.

The clinical diagnostic criteria for coarctation (adult type) are: (Oppholzer [1848][6]) (1) differences in pulse volume (palpable) between radial and femoral arteries; absence or minimal pulsation of the abdominal aorta; (2) evidence of arterial collateral circulation on chest and abdomen; (3) aberrant systolic noises on chest (Laubry [1926][7]); (4) difference in pulse and systolic pressure between arm and leg, the pulse and systolic pressure being higher in the arm (Railsback and Dock [1929][8]); (5) x-ray evidence of erosion (scalloping) of the ribs.

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CASE REPORTS

CASE 1.—C. S., aged thirty-two years, male, entered the hospital December 31, 1928, discharged January 16, 1929. The patient was sent in for thyroidectomy. Two basal metabolic rates taken at intervals—the latter, one week before admission—were plus 42.

Present Illness: Onset six years ago—dizziness, shortness of breath, palpitation. Hypertension noted six years ago. He tolerates heat well but suffers from the cold. There has been puffiness of the face and hands. During the last three months he has taken Lugol's solution, minims 10, three times daily. The patient was referred to surgery because of the request of his physician, and because he had a thrill over the enlarged thyroid, tremor of the fingers on extension of the hands and a history of increased basal rate readings. A hypertension, recorded as 210/134 mm., was noted, and there was also an enlarged heart with a systolic murmur at the apex which was not transmitted.

The family history is unimportant except perhaps for the fact that the mother died of apoplexy (age not stated). The patient is married. His wife and children are well. He has diseased tonsils and cervical adenopathy, also pansinusitis (x-ray).

When seen by Dr. Karl Anderson of the medical staff it was noted that there was a "mass" under the sternum, a to-and-fro extracardiac murmur heard in the back at the angle of the scapula, also several pulsating vessels in the back. The diagnosis was at the time "hypertension," "mass in upper part of the thorax." "hyperthyroidism, questionable." "Operation should be deferred for more accurate study and to obtain a better understanding of extracardiac murmurs." On comparing the radial pulsation with the abdominal and femoral pulsations a striking difference was noted. Further observation of this man revealed, besides the marked pulsation of the arteries of the neck, the visible pulsation of vessels in the back along the vertebral border of the scapula and palpable vessels which pulsated along the intercostal spaces. When this patient became quieter, no cardiac murmurs were audible. A systolic bruit in the neck vessels was heard and there was a postsystolic murmur in both interscapular areas at the level of the second and third thoracic vertebrae. Deformity of the spine (scoliosis) was noted. The mass under the sternum was interpreted as an enlarged vessel off the arch, because retrosternal dullness varied under rest.

Eye grounds—arteriosclerosis, tortuosity of vessels. Kidney function normal. Blood and urine normal. Basal metabolic rate on January 5, plus 4. Electrocardiogram, January 8, 1929—normal complexes, T in Lead I flat.

Blood pressure readings in arms and legs:

		Left	*Right*
March 3, 1929	Arm	186/108	194/112
	Leg	124/118	114/ ?
April 14, 1929	Arm	190/120	188/120
	Leg	120/110	120/110
May 24, 1929	Arm	168/102	170/102
	Leg	130/120	120/92
January 26, 1930	Arm	208/120	198/126
	Leg	140/120	140/118
May 18, 1930	Arm	220/115	210/115
	Leg	140/125	140/120

Physical findings on January 26, 1930, about one year after discharge from the hospital: Congestion of face and slight cyanosis. Pupils equal, react to light and accommodation. Some visible pulsation of vessels of the neck. Some venous

dilatation. Some asymmetry of thorax—left bulges slightly, moves freely. Some cardiac enlargement. Abdomen is normal. Extremities of good color, veins are quite numerous and visible. Percussion of thorax—clear, no retrosternal dullness found. Patient feels well. Has no roaring in his ears, no headaches. Legs tire when he goes upstairs. Arm and leg pressures noted in table of pressures.

The patient had been working steadily for one year at fairly hard labor in a steel mill.

X-ray Report (Dr. Rigler): January 5, 1929, Ad 6390, Chest and Spine: Fluoroscopic and film examination of the thorax was made. There is a shadow in the superior mediastinum which pulsates slightly. This may be due to a substernal thyroid, but its appearance is not characteristic, and the possibility of its being due to dilated vessels cannot be ruled out. The heart appears to be within normal limits in size, shape and position, but there is a marked distortion of the spine which causes the heart to protrude to the left side. Only the arch and ascending aorta can be fairly visualized. The descending aorta was not well visualized. Plates of the spine reveal multiple deformities, the third and fourth dorsal vertebrae being used together, and the seventh and eighth being very much deformed. Its appearance is characteristic of a congenital lesion, and suggests intercalation. A further study of the spine is advisable. There is a marked deformity of the ribs on the right side, secondary no doubt to the spinal deformity and some scoliosis. Erosion of the ribs along their inferior margins is shown. This is characteristic of dilated pulsating arteries. *Conclusions:* Congenital deformity of spine. Possible substernal thyroid. Possible dilated vessels of neck. Erosions of ribs secondary to dilated intercostal vessels.

January 29, 1930, Ae 864, Chest: Reexamination of the chest and heart with the barium filled esophagus was made. The findings are much the same as last reported. There is little or no distortion of the esophagus except that it is displaced somewhat to the right in the anteroposterior view just below the arch of the aorta. The aorta could not be clearly visualized and suggests an atresia. The distinct erosion of the ribs previously reported is again shown and is due to pulsation of the tortuous intercostal vessels. The deformity of the spine previously reported is again shown. *Conclusions:* Multiple congenital deformities of spine. Erosion of ribs secondary to tortuosities of intercostal arteries. Distortion of esophagus secondary to abnormality of aorta. Enlarged heart, left ventricular type.

Comment: The x-ray report of erosion of the ribs in this man with the correct interpretation of its cause, was made previous to our knowledge of the publication of Railsback and Dock's[8] article. It was decided at the time of the observation to wait for verification of this finding in other cases before calling attention to it. This was neatly done by Railsback and Dock. The syndrome of hyperthyroidism in this case and its appearance in cases of coarctation are discussed subsequently.

Case 2.—Miss S., aged twenty-one years, patient of Dr. M. W. Alberts, St. Paul.* The patient was seen in January, 1930. She is a young woman in apparently good health attending the university. She gives a history of having had symptoms of hyperthyroidism five and a half years ago. Thyroidectomy was performed without results. One year later another portion of the thyroid was removed. This improved the patient's nervous symptoms but did not relieve her hypertension which had been present throughout this period. It was then noted and there was a marked

*We again take occasion to thank Dr. M. W. Albert for his permission to use this case as clinical material and for the opportunity to mention it in this report.

difference in pulsation of the brachial and femoral arteries. The diagnosis of coarctation was made. Since her operation four years ago she has been slightly restricted in her activities.

Physical Examination: The patient is a well-nourished, well-developed young woman. There is a full thyroid; the vessels pulsate in the neck but there is no thrill. The heart is not enlarged. All over the chest a systolic bruit is heard. Besides this, cardiac sounds are well heard all over the chest. Along the sternum on the right a systolic murmur is heard which can be traced far down the abdomen to the level of the umbilicus. A similar murmur is heard on the other side of the abdominal wall. Along the right axillary area this systolic murmur is pronounced. In the back, pulsation of intercostals can be made out on palpation from midscapular area to as low as the ninth interspace on both sides. A systolic bruit is heard along the inner margin of the scapula on both sides. The characteristic interscapular systolic noise is not so obvious as in Case 1. There is absence of palpable pulsation in the abdominal aorta and very feeble pulsation of the femorals.

Eye grounds, beginning arteriosclerosis, tortuosity of the vessels. Blood pressure readings:

		Left	*Right*
January, 1930	Arm	190/100	200/110
	Leg	130/110 difficult	130/110
In May, 1930	Arm	170/90	170/90
	Leg	128/100	120/95

X-ray Report: February 3, 1930, Ae 1023, Chest and Esophagogram (Dr. Rigler): The heart shows only a very slight enlargement, chiefly in the left ventricle. The aorta shows some slight dilatation of the ascending portion, but the arch is small and the descending portion can be very poorly visualized. It can, however, be made out. A definite area of constriction in the aorta cannot be clearly visualized. There is no particular distortion of the esophagus. A definite erosion on the inferior surfaces of the ribs on both sides extending down to the eighth rib posteriorly is clearly made out. This is characteristic of the type of erosion which is clearly made out. This is characteristic of the type of erosion which is due to tortuosities of the intercostal arteries. There is a shadow in the superior mediastinum very ill-defined but suggesting enlarged dilated vessels. *Conclusions:* Slight cardiac enlargement, left ventricular type. Erosion of ribs from pressure of vessels; coarctation of aorta (clinical).

Comment: Blackford[2] reported this case, we assume as No. 7. Since he gave no differential blood pressure readings nor mentioned the erosion of the ribs, we have incorporated this data. This is the second case which has come to our notice presenting at some time in the history evidence of a hyperthyroid complex. The possible explanation for this will be given in the discussion.

Case 3.—O. J., aged twenty-three years, admitted March 6, 1930.

Present Illness: The patient felt very well until February, 1929, when he developed an inguinal hernia on the right side. This did not trouble him very much so he did light work. The hernia increased during the summer of 1929. He worked in the harvest fields in the fall of 1929. He felt very well when lying on his back and the hernia was reduced. Swelling of the abdomen began in February, 1929. It was gradual and painless. No jaundice was noticed at the time. There was no edema of the ankles, no dyspnea, no cyanosis. He was confined to bed for one month before admission.

Past History: His previous health had been good. Apparently he had a normal childhood. He ran and played with the other children. He never was short of breath. The mother noticed that he was usually pale. He never flushed when running. He catches "cold" easily. There have been no headaches, no palpitation. No dyspnea was noticed until six weeks before admission. There is no history of rheumatism. The family history is negative.

Physical Examination: On admission there was slight dyspnea, and he was able to lie flat in bed without discomfort. Sclera icteric; slight acrocyanosis. Thorax: Lungs clear; marked enlargement of the heart to the right and left; shape of the heart probably altered by intra-abdominal pressure. A rough systolic thrill was felt at the apex. At the base there was a rough diastolic murmur occupying the whole of diastole evident in the pulmonic area. No other murmurs were noticed. Pulse 41 to 56; occasional extrasystoles. Blood pressure 154/96 mm. Abdomen: Marked ascites; liver down to umbilical level. Liver seems firm, not tender. Spleen not felt. Right inguinal hernia with fluid, easily reducible. Extremities: Reflexes diminished. Slight edema of the legs. Slight cyanosis; radials sclerotic. No clubbing of fingers present.

Paracentesis on March 7, 1930: Liver now made out as enlarged, with round hard edge; surface feels granular. Spleen palpable and hard. Lungs clear. Heart: Murmurs have changed; now a rough systolic murmur was heard over the base. Pulsation was made out on vessels of the back particularly along the vertebral borders and in the intercostal spaces. Pulsation of the abdominal aorta was not found. Pulsation of the femorals was very faint. The ascites was controlled by novasural and ammonium chloride. On March 29 the patient was up and about. No edema of the legs. On sitting up, there was systolic retraction at the apex. On palpation a short rough thrill was felt at the apex.

Paracentesis on April 30, 1930: Murmurs at base have disappeared. Posteriorly the murmurs persist "postsystolic in time." The point of greatest intensity of this murmur is at the level of the third thoracic spine but can be heard as far down as the seventh spine in both intrascapular spaces. The pulsation of the neck vessels was very forceful but did not have the celerity felt in the other cases of coaretation we have seen. In fact, at times the radial pulse suggests aortic stenosis. There was a systolic retraction in the lower intercostal spaces on the left, in the axillary line. Conjunctivae were slightly yellow.

Eye Grounds: "O. D. vessels, particularly the smaller arteries and veins, very tortuous; some change in vessel walls, particularly arteries. O. S. similar to O. D. Tortuosity of small vessels marked." (Dr. Lane.)

Laboratory: Blood normal. Icterus index March 11, 1930: 12. Icterus index May 7, 1930: 20. Urine: Urobilin, P. S. P. 80 per cent two hours. Electrocardiogram March 11, 1930: Bradycardia, left bundle-branch block.

Blood pressure ranged from 154/96, 144/86, to normal readings in arms. Leg readings were not obtainable. In September, 1930, readings were obtained in his legs.

	Left	*Right*
Arm	140/78	140/82
Leg	104/90	104/90

X-ray Reports: March 10, 1930, Ae 1894, Six-foot Chest (Dr. Rigler): The heart is greatly enlarged to the right and left with a marked bulging in the region of the conus pulmonalis and considerable enlargement of the left ventricle. The aorta is very poorly visualized, especially in its ascending portion, but even in the descending portion it is very difficult to make out. There is evidence of a marked pulmonary congestion on both sides. The diaphragms are very high. A definite erosion of the inferior surface of the posterior ribs is shown, characteristic of

coaretation of the aorta and due to the enlarged intercostal vessels causing pressure on the ribs. The esophagus shows a definite posterior displacement due to enlargement of the left auricle. Otherwise there is little or no evidence of change.

After evacuation of the fluid from the abdomen, the diaphragm has come down somewhat, and the heart does not appear quite so enlarged but is still massive, and the pulmonary congestion is still very prominent. The findings in the ribs are again shown, and the marked enlargement of the left auricle is definitely shown. The whole appearance suggests a coaretation of the aorta with some other lesion in addition, the appearance suggesting most strongly a marked degree of mitral disease in addition to the aortic disease. There is a marked enlargment of the left ventricle also.

Operations: May 14, 1930. Talma-Morison operation under spinal anesthesia. Piece of the liver examined microscopically. Report of frozen section: cirrhosis of the liver (Bell). (There was a slight infection of the bronchi following this operation; temperature 102°; leucocytes 15,500.) No pulsation on direct palpation of the aorta reported by the surgeon (Wangensteen) at the time of the operation.

June 13 to 18, tapping of hydrocele.

Discharged June 24, 1930; patient up and about.

Reentered hospital November 4, 1930. Died November 7, 1930.

After the Talma-Morison operation there was relief of ascites for a brief period. The patient was up and about. The abdomen was tapped at intervals of two and three weeks after leaving the hospital in June. On October 25, 1930, the patient had an attack of weakness, he was conscious of his heart (''pounding fast'') and some precordial pain. The attack lasted eight minutes. He has had similar attacks since. These attacks never last more than ten minutes. After each attack the patient feels weak temporarily. Between attacks he does not ''know he has a heart.'' His general health, appetite, sleep, and bowels were normal.

His physical examination on November 4, 1930, revealed no new data. When seen in one of his attacks his heart was very rapid and irregular. There was dyspnea, cyanosis and sweating. Venesection was done in his fatal attack. Two minutes after venesection the patient gasped suddenly, vomited, and his respiration became spasmodic. The heart stopped before respiration. Electrocardiogram some five hours earlier had shown tachycardia, rate 200, possibly nodal in origin.

Necropsy (Dr. O'Brien.)—O. J., A 31-1662. The body is that of a young white male, 175 cm. in length, weighing approximately 165 pounds. Nutrition and development are good. No edema or jaundice. The abdomen is distended. The veins over the anterior and lateral chest wall and abdomen are prominent.

The peritoneal cavity is filled with 6000 c.c. of clear straw colored fluid. The liver is firm and extends well below the costal margin.

The pleural cavities are free of adhesions and effusion. The pericardial sac contains approximately 100 c.c. of clear straw colored fluid.

The heart shows generalized enlargement. It weighs 870 grams. It is 20 cm. in width, the thoracic width at this level being 27 cm. All chambers are enlarged, especially on the right. The left ventricular walls vary from 1.5 to 3 cm. The right varies from 1.0 to 2.0 cm. in thickness. The auricular walls are thickened and distended. The mural endocardium is smooth and shows no thrombosis. The valve edges are free and leaflets are thin. The interauricular and interventricular septa are intact. The coronary arteries show slight internal atheromatous deposits, but no interference with the lumina. There are diffuse yellowish deposits in the pulmonary artery, root of the aorta, base of the aortic valve and the aortic leaflet of the mitral valve. The muscle is slightly cloudy but shows no evidence of fibrosis.

The aortic arch rapidly tapers down to a moderate constriction proximal to the left subclavian artery. There is a more marked constriction near the junction

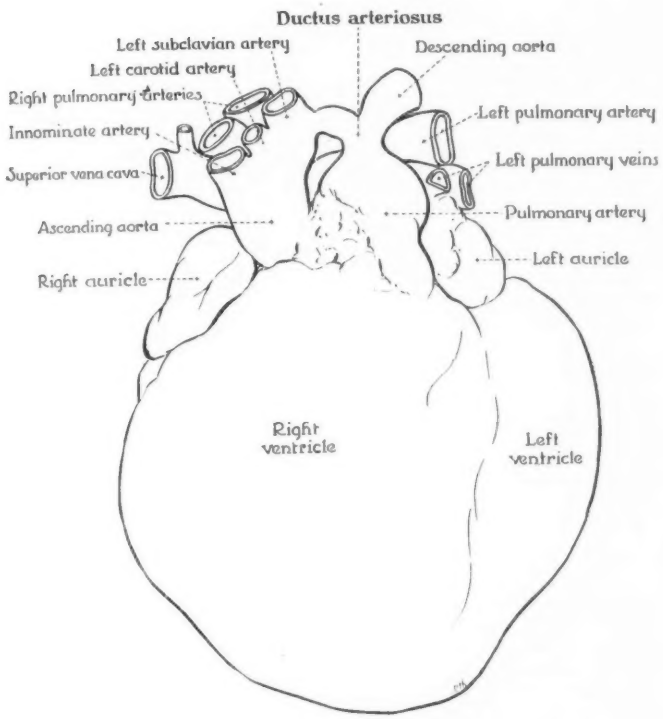

Fig. 1.—Viewed from above and slightly to the left, this drawing is an excellent proportionate outline of the heart and vessels. The arch is somewhat displaced to the left due to fixation. The descending aorta is also distorted by the removal of the specimen from the body and by fixation. The narrowing beyond the left subclavian is marked but does not give an adequate idea of the extent of the atresia because the vessels have not been opened. (See report of the pathologist.)

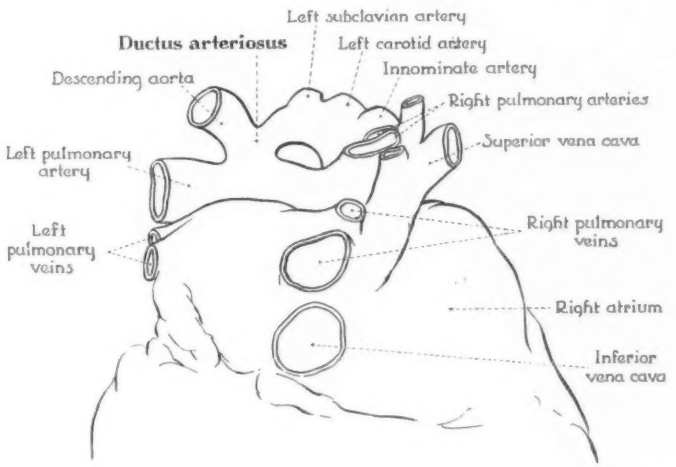

Fig. 2.—Viewed from below and behind. The same distortions of the arch and descending aorta (for similar reasons as in Fig. 1) are noted.

of the arch with the descending portion. The ductus arteriosus is patent and connected with aorta, at the site of the marked constriction. A probe is passed through the ductus arteriosus and passes readily into the descending aorta. It is practically impossible to pass a very fine probe through the distal stricture of the aorta. The descending aorta is smaller than normal. There is a dilatation of the proximal portion of the descending aorta for a distance of 5 cm. Beyond this it is uniformly narrowed, averaging 1 cm. in diameter. The common iliac vessels are smaller than normal but show no other abnormalities. The left carotid is normal in size. The left subclavian artery is dilated and thickened. The innominate artery is distended and has a thin wall. All of the intercostal vessels are markedly dilated, thickened and tortuous. The change is most marked in the first intercostal vessel on the left side. This vessel is approximately the same size as the right carotid artery. Both subclavian arteries are marked dilated. The internal mammary arteries are dilated and tortuous. The axillary arteries are apparently normal in size. The pulmonary artery and conus are markedly dilated. The two pulmonary arteries arise from the posterior superior portion of the distended trunk. The pulmonary vessels show no dilatation nor sclerosis.

The spleen weighs 500 grams and is definitely enlarged. The surface is covered with a diffuse hyaline change. Multiple adhesions between the spleen and stomach and abdominal wall are present. On cut section marked chronic passive congestion is found.

The liver weighs 2,725 grams. Slight hyaline perihepatitis is present, and the surface is roughened due to the liberation of adhesions. The organ is firmer than normal. On cut section marked darkening of the centers of the lobules is seen. There is increased resistance probably due to fibrous tissue deposits. Slight fatty metamorphosis is present throughout.

The right kidney weighs 230 grams and the left 250 grams. The capsules strip without difficulty, and the presenting surface is dark red and hemorrhagic in appearance. There is faint fine pitting over the surface. Section shows the cortices of fairly uniform width.

Microscopic Examination: Sections of the heart muscle are normal. No evidence of pulmonary arteriosclerosis is seen. The spleen shows marked chronic passive congestion. The liver presents marked congestion and atrophy of the cords in the liver lobule, especially in the central portion. There is a moderate increase in the portal connective tissue and lymphocytes, presenting the picture of a moderate portal cirrhosis. The kidneys are carefully studied from the standpoint of possible arteriolar sclerosis but none is found.

Diagnosis: (1) Coaretation of the aorta. (2) Patent ductus arteriosus. (3) Marked dilatation of the subclavian, carotid, innominate, internal mammary, intercostal and pulmonary arteries. (4) Marked narrowing of the descending aorta and common iliac arteries. (5) Cardiac hypertrophy and dilatation. (6) Chronic passive congestion of all viscera. (7) Ascites. (8) Portal cirrhosis. (9) Vascular adhesions of the stomach, spleen, liver and peritoneal cavity (operation).

ASSOCIATED ANOMALIES

Case 1 had a spinal deformity in the thoracic area; the third and fourth ribs were pressed together and the seventh and eighth being much deformed having on the right an intercalated vertebra with an an extra rib. This type of somatic deformity is new, using Maude Abbott's[3] report as a criterion.

The aorta in Case 3 certainly suggests aplasia, although the pathologist does not stress this point.

DISCUSSION

While the clinical criteria are sufficient to make a diagnosis, hemiplegia, or symtoms of hyperthyroidism with increased blood pressure in the young should make one alert as to the possibilities of coaretation. Two of our three cases had evidence of hyperthyroidism. Both Case 1 and Case 2 had definitely increased metabolic rates. In Case 2 the patient had her thyroid operated on twice before she was pronounced normal. Case 1 escaped surgical interference. Rest, with assurance that his condition had been properly diagnosed, and the withdrawal of Lugol's solution reduced the patient's metabolic rate to normal. Lorrigia[9] was the first to mention, and Blackford[2] later noted, hyperthyroidism in connection with this defect. Is the overactivity of the thyroid due to the increased vascularity of the gland? There is an apparent increase of blood flow in the areas above the clavicles. The inferior thyroid comes off the subclavian. The subclavian and its branches are the usual arteries of collateral circulation. That increased blood supply may be a factor in the overactivity of the thyroid in these cases is a reasonable hypothesis. That it may be a factor in other cases reported with this defect is also a legitimate assumption. If this is correct, then ligation of the inferior thyroid may be all that is necessary to relieve the hyperthyroid symptoms in some of these cases.

All three cases, aged respectively nineteen, twenty-two and thirty-one years, had evidence of tortuosity and beginning arteriolar changes in the retina. If, in essential hypertension, arteriolar changes of the vessels in the retina are indicative of arteriolar changes in the vessels leading to the glomeruli in the kidney (Bell), it would be of interest to examine the preglomerular vessels in these cases as they come to the postmortem table. Our single postmortem examination showed no changes in the kidney.

Students of vascular pathology have an important and striking "set up" in these coaretation cases to study the effect of work or tension, plus wear and tear or pulse pressure in the upper part of the body as compared with work or tension in the lower part. It is to be noted that in these three cases while the systolic pressure in the arm is higher than in the leg, the diastolic is the same or even higher in the leg. In other words, there is hypertension in the lower extremities. The observations of Blumgart et al.[10] differ on this point. In one case their readings given for the lower extremity show a lower diastolic pressure than normal. In their second case no diastolic readings in the leg are given. All of our readings were made with a 20 cm. cuff. We found a high normal diastolic (90 mg. of mercury) or above. Blumgart's arteriolar pressures were normal in the legs. Is the high diastolic pressure in the lower portion of the body a compensatory phenomenon to insure adequate arteriolar pressure?

Those interested in the pulse may learn something for or against

their theories as to the factors in its mechanism. The pulse is a distention of the wall of the vessel induced by the increased volume of blood propelled by the systolic force of the heart. In Case 3, during the operation for relief of his portal circulation, the surgeon had an opportunity to feel the aorta in the abdomen. He reported there was no pulsation. I know of no other observation of its kind in coaretation. That this is a constant finding cannot be true. It was usually difficult to get the blood pressure readings in the legs in Case 3, but occasionally they were obtainable. If there was a pulse pressure in the femorals at times, there must have been a pulse in the abdominal aorta at those times. The loss of pulse in Case 3 was due to extreme atresia and the dissipation of the systolic wave in the collaterals. That there was adequate supply of blood flow must be conceded. Not one of these three cases had symptoms of weakness(atrophy or loss of function in the legs. Blumgart et al. suggest from their blood gas studies a low gas reserve in the legs.

All three cases showed the characteristic erosion of the ribs described by Railsback and Dock.[8] This finding has been confirmed by others. The relation of age to the appearance of this defect is pertinently discussed by Fray.[11] If we look on page 385 of THE AMERICAN HEART JOURNAL, Vol. 3, 1927-28 (Hamilton and Abbott[3] "Coaretation of the Aorta"), the x-ray plate of the fourteen-year-old boy shows some of the characteristic erosions of the ribs. Realizing the fact that erosion is not an absolute pathognomonic sign, we have studied the esophagogram and its relation to the arch, without any definite results. We do not wholly agree with Fray that the main reliance (roentgenologically speaking) should be placed on the defect in the arch in the left oblique view.

SUMMARY

Three cases of adult type of coaretation are reported. The postmortem findings are given in one case.

Case 1 had a somatic anomaly, involving the thoracic vertebrae. This has not been reported previously in the literature.

The cirrhosis of the liver in Case 3 may have had a basis in the modified blood supply.

The diagnostic importance of x-ray evidences of erosion (scalloping) of the ribs is emphasized.

The findings of increased basal metabolic rate in two cases is mentioned. A possible explanation is suggested for this increase.

Attention is called to the "set up" which these cases afford for the study of vascular problems. The work (tension) in the vessels, plus increased pulse pressure in the head, neck and arms, as contrasted with work (tension) without pulse pressure in the legs is stressed. In the patient who died the arterioles of the eyes (clinical) and kidneys (anatomical) are compared.

Attention is called also to the high diastolic pressure in the legs. The impression from these three cases is that this is a compensatory phenomenon.

REFERENCES

1. Abbott, M. E.: Coaretation of the Aorta, Osler's Modern Medicine, D. Appleton & Co., New York, 1926.
2. Blackford, L. Minor: Coaretation of the Aorta, Arch. Int. Med. **41**: 702, 1928.
3. Hamilton, W. F., and Abbott, M. E.: Coaretation of the Aorta, Adult Type, Am. Heart J. **3**: 381, 1928.
4. Dally, J. T. Hall: The Diaphragm in Man, St. Bartholomew's Hosp. Rep. **44**: 161, 1908.
5. Keith, A: Proc. Anat. Soc. of Great Britain & Ireland, 1902. J. Anat. & Physiol. **33**: 259. New Series **14**: 25, 1902.
6. Oppolzer, Johann von (Quoted by Barié E.): Du rétricissement congenital de l'aorte deseendante. Rev. Méd. **6**: 324, 1886. Reported by Hamernjk, Vierteljahrschrift f. du. Prakt. Heilkunde, 1848, p. 40. See also p. 65.
7. Laubry, Chas.: Bull, et. mem. Soc. Méd. d. hôp. de Paris **50**: 1725, 1926,
8. Railsback, O. C. and Dock, W.: Erosion of the Ribs Due to Stenosis of the Isthmus (Coaretation) of the Aorta, Radiology **12**: 58, 1929.
9. Lorrigia, G.: Stenosi ed obliteraziona congenita dell' aorta, Riv. Clin. di Bologne **7**: 529, 1887.
10. Blumgart, Herman, Lawrence, John S., and Ernstine, A. Carlton: The Dynamics of the Circulation in Coaretation (Stenosis of the Isthmus) of the Aorta of the Adult Type, Arch. Int. Med. **47**: 806, 1931.
11. Fray, Walter W.: The Roentgenological Diagnosis of Coaretation of the Aorta (Adult Type), Am. J. Roentgenol. **24**: 349, 1930.

THE ACTION OF ADRENALIN ON PATIENTS WITH COMPLETE HEART-BLOCK AND STOKES-ADAMS SEIZURES

A Comparison of the Effects of the Drug on Patients With Syncopal Attacks Due to Standstill of the Ventricles and Those Due to Ventricular Fibrillation*

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THE purpose of this study was to determine the effect of adrenalin on the heart rate and rhythm of patients with auriculoventricular dissociation subject to Stokes-Adams seizures. It is now definitely established that recurrent syncopal attacks in such patients may be the result of either ventricular slowing and standstill[1] or of the various grades of acceleration of the ventricles leading to transient ventricular fibrillation.[2] While there are now some excellently controlled observations on the action of adrenalin in patients with auriculoventricular dissociation and standstill of the ventricles, both preceding and during the presence of syncope, there are no comparable analyses of the cardiac mechanism following the use of the drug in patients subject to transient periods of ventricular fibrillation. This is of particular importance at the present time, since adrenalin is being prescribed indiscriminately in patients with Stokes-Adams seizures without any knowledge of the mechanism responsible for the attacks.

REVIEW OF THE EXPERIMENTAL OBSERVATIONS

In studying the distribution of the nerves of the heart, Cullis and Tribe[3] noted an increase in the rate and force of contraction of both the auricles and ventricles in cats and in rabbits in which they injected small doses of adrenalin before and after section of the auriculoventricular bundle.

These findings were subsequently confirmed by Van Egmond,[4] who noted an increase per minute of 15 beats in the ventricular rate and 30 beats in the auricular rate following the use of adrenalin in dogs with their vagi intact.

In a dog with a crushed auriculoventricular bundle, Routier[5] injected intravenously, 1/20 mg. of adrenalin and within twenty seconds observed an increase in both the auricular and the ventricular rates. Twenty seconds later there was a disappearance of the complete heart-block which lasted for twenty-five seconds. Routier was able to reproduce this experiment three times on the same animal and suggested the use of the

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drug in human heart-block because of its possible value in establishing normal rhythm and not because of its effect on the ventricular rate.

In a similar experiment Hardoy and Houssay[6] failed to establish normal rhythm in a dog with complete auriculoventricular dissociation with 0.2 c.c. (1/5 mg.) of a 1:1000 solution of adrenalin. They noted, however, an acceleration of both the auricular and ventricular rates as well as the appearance of premature ventricular beats.

REVIEW OF THE CLINICAL OBSERVATIONS

The first observations on the effects of adrenalin on patients with complete heart-block are those reported by Danielopolu and Danulescu.[7] In a man fifty-seven years of age with auriculoventricular dissociation and recurrent syncopal seizures, whose ventricular rate varied from 26 to 40 beats per minute, the injection of 1 mg. of adrenalin resulted within three or four minutes in an increase of both the auricular and the ventricular rates as well as the onset of premature ventricular beats. In a subsequent communication the same authors claimed to have been able to abolish a partial heart-block by means of this drug.[8]

Hardoy and Houssay[6] observed a similar acceleration of both the auricular and the ventricular rates one minute after the intravenous injection of 1 c.c. (1 mg.) of a 1:1000 solution of adrenalin in a man fifty-five years of age, with auriculoventricular dissociation and a regular ventricular rate of 30 to 32 beats per minute. Five minutes later there was a return to normal of both the auricular and the ventricular beats, but the P-waves of the electrocardiograms were at times negative. They quote Arrilaga[9] who observed the same phenomenon in several cases with auriculoventricular dissociation. None of these authors mention that their patients were subject to Stokes-Adams seizures.

Lutembacher's observations[10] with polygraphic tracings are of greater interest. He injected 0.5 mg. of adrenalin in a patient with auriculoventricular dissociation and a basic rate of 25 to 30 beats per minutes, and produced violent constriction of the chest which was followed by a "ventricular pause with syncope." The face became pale and this was followed by intense cyanosis with distention of the veins; then, after a short period of unconsciousness, there was a sudden increase in the ventricular rate to 84 beats per minute, which became regular when the patient regained consciousness. Seven minutes after, the heart beat at the rate of 40, but the patient still complained of severe precordial constriction. Twenty minutes later, the rate was still 40 and there was mental confusion, but on the following morning the patient's sensorium was clear and the pulse was 18. A second intravenous injection to this patient of 0.25 mg. of the drug, when the basic auricular and ventricular rates were 75 and 28, respectively, resulted in an immediate acceleration of the auricles to 85 beats and the ventricles to 75.

In another similar case the intravenous use of 0.1 mg. of the drug was followed by premature beats of the ventricles, tachysystole and finally cessation of "ventricular activity." Ten minutes after the injection both the auricular and the ventricular rates returned to normal. For eight days following this experiment the ventricular rate averaged 16 beats per minute.

In 1920 Strissower[11] injected adrenalin in a patient with complete auriculoventricular dissociation and noted an increase in the ventricular rate with a temporary return to normal rhythm. One month later, when the patient showed a partial heart-block with a two-to-one rhythm, the drug abolished the block, but only for a few seconds.

Two years later, Phear and Parkinson[12] studied a woman of forty-nine years with complete heart-block and frequently recurring syncopal seizures, in whom the subcutaneous injection of adrenalin was followed by complete cessation of the attacks within fifteen minutes. They suggested an extended trial of adrenalin in patients with Stokes-Adams seizures when the immediate loss of consciousness is normally due to extreme slowing and standstill of the ventricles, for these may be abolished by the increase in the ventricular rate due to the drug.

A somewhat similar case was reported by Feil[13] who noted cessation of syncopal attacks in a man fifty-six years of age with complete auriculoventricular dissociation, following the administration of 0.4 mg. of adrenalin. The attacks recurred twelve hours later and again twenty-four hours afterward, and on each occasion they were stopped by a similar injection.

In a man, aged forty-four years, with a rapidly increasing heart-block which became complete after thirty hours, Parkinson and Bain[14] used adrenalin on twelve separate occasions following the onset of Stokes-Adams seizures, and each time the drug abolished the attacks within three minutes. Freedom from attacks was maintained from two to forty-eight hours from the time of injection. On four occasions when partial block was present there was an increase of both the auricular and the ventricular rates with restoration of normal rhythm. At one time there was no increase in the ventricular rate with the use of the drug when the block was complete, while at another time there was definite increase.

In a woman, fifty-six years of age, Korns and Christie[15] injected intramuscularly 0.7 mg. of epinephrin and produced an increase in the auricular and ventricular rates, a marked auricular arrhythmia and many premature ventricular beats as well as an increase in the auriculoventricular block when the block was partial.

In summarizing the clinical results to date, the evidence shows that adrenalin in doses of from 0.3 mg. to 1 mg. when administered subcutaneously, intramuscularly or intravenously may accelerate both the auricular and the ventricular rates of patients with auriculoventricular

dissociation whether they are subject to Stokes-Adams seizures or not. The increase in rates may be regular or irregular. When the vagal effects of the drug predominate, the auricles may be slowed at first, and in patients with partial heart-block the block may be augmented. In a few instances normal rhythm could be established. In a small group of patients in whom syncopal seizures were found to be due to standstill of the ventricles, the drug was found to cause a cessation of the attacks, with or without an increase in the rate of the ventricles. In several instances, however, the use of the drug was followed by "syncope" with what appeared to be stoppage of the ventricles. For this unusual response no explanation has as yet been offered.

METHOD OF PROCEDURE

A 1:1000 solution of adrenalin was administered subcutaneously and intramuscularly in graded doses ranging from 0.3 mg. to 1 mg. to four patients with complete auriculoventricular dissociation suffering from transient syncopal seizures. In one patient an intracardiac injection was performed.

There were two males and two females. The heart-block in these patients was due, in all probability, to disease of the conduction system following coronary vessel closure. In the male patients it was definitely established that the syncopal attacks were the result of a marked slowing of the ventricular rate, whereas in the female patients the mechanism responsible for the attacks was found to be due to the various grades of ventricular acceleration leading to ventricular fibrillation.[2, 16] All of these tests were carried out at a time when the patients were known to be free from seizures for several days and when both basic auricular and ventricular rates were fairly constant and did not vary more than an average of 8 beats per minute.

In two instances also the drug was given during a syncopal seizure. The adrenalin was administered to the patients while they were in the electrocardiographic circuit, and records were taken as frequently as was thought necessary. During this time detailed notes were made of the patient's general reaction to the drug as well as of the clinical rate and rhythm of the pulse. Observations were discontinued in each instance four hours following the injections. Tests were not repeated on the same patient in less than two days.

RESULTS OBTAINED IN PATIENTS WITH COMPLETE AURICULOVENTRICULAR DISSOCIATION AND SYNCOPAL ATTACKS DUE TO VENTRICULAR STANDSTILL

In the two male patients in whom the syncopal seizures were due to a marked slowing of the ventricular rate, the intramuscular administration of 0.3 mg. of the drug resulted within three to five minutes in a progressive increase of the basic auricular and ventricular rates from an average of 78 and 34 beats per minute to 114 and 48 respectively. Ten minutes later the pulse rate was noted to be slightly irregular, and this was found to be due to an irregular spacing of the idioventricular beats and not to premature beats of the ventricles. The greatest increases in these rates were observed to come on from eight to ten minutes later. The patients at no time complained of any systemic symptoms, such as marked tremor, sweating, nervousness or palpitation of

the heart. The heart rates returned to their normal basic level within one-half hour after the injections.

The use of 1 mg. of adrenalin on a different occasion resulted in similar changes. Within one minute, the progressive accelerations in the rate described above began to appear, and these lasted a little over one hour and again there were no accompanying general disturbances.

In one patient, at a time when there was a slowing of the ventricular rate to 6 beats per minute with syncope which lasted for three minutes, the injection of 1 mg. of the drug intramuscularly, resulted within two minutes in a progressive acceleration of the ventricles. Ten minutes later these averaged 80 beats per minute and were regular. One hour later the ventricles returned to their normal basic rate of 24 beats after passing through a variable stage of irregularity consisting of an unequal spacing of the ventricular beats which, however, were all felt to come through at the pulse.

Premature ventricular beats were not recorded in them at any time during the use of adrenalin.

RESULTS OBTAINED IN PATIENTS WITH COMPLETE AURICULOVENTRICULAR DISSOCIATION AND SYNCOPAL ATTACKS DUE TO VENTRICULAR FIBRILLATION

The sequence of events following the use of adrenalin in the two patients in whom syncopal seizures were due to ventricular fibrillation was very variable.

The subcutaneous administration of 0.3 mg. of the drug resulted within three minutes, at one time, in an acceleration of the basic ventricular rate from an average of 38 beats per minute to 46. The auricular rates were barely influenced. Similar results followed the intramuscular injection with the same quantity of the drug, but the increase in the ventricular rate appeared after one minute and lasted fifteen minutes.

On another occasion the subcutaneous administration of 0.5 mg. of adrenalin was followed in one patient by an unusual sequence of events which deserves a detailed description.

Before the injection the basic ventricular rate was regular and averaged 26 to 28 beats per minute. The auricular rate was 73 beats per minute (Fig. 1 *A*). The auricular complexes of the electrocardiogram were upright and alike from beat to beat. The ventricular complexes were also upright but varied occasionally in size, shape and form.

One and a half minutes after the injection, the pulse at the wrist began to show coupling which persisted for twenty seconds and then there was a sudden pause. On listening over the apical region four distinct but progressively weaker heart sounds could be heard preceding this pause. At the same time the patient's eyes closed, she lost consciousness, the face assumed a deathly pallor which was followed by

intense cyanosis, and this changed suddenly to a bright red flush of the face which coincided with a heart beat coming through at the pulse. This whole period lasted only fourteen seconds, following which the pulse became regular again for about another one and one-half minutes.

The electrocardiograms recorded during the period of clinical bigeminy (Fig. 2), showed the auricular rate to be 75 beats per minute and regular and the complexes all of the upright form. The complexes of the basic ventricular rhythm were of high voltage (Fig. 2 *A*, *B*) as compared with those prior to the use of the drug and, the T-waves were of unusual shape and form, becoming progressively larger in size from beat to beat (Fig. 2 *C*, *D*, *E*).

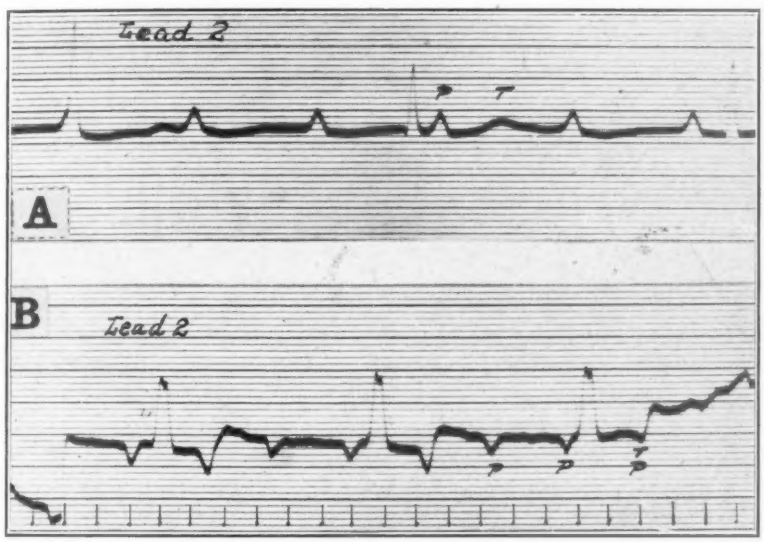

Fig. 1.—(The time in all of these records is in fifths of a second.) *A*, Before the injection of adrenalin, the auricular rate was 73 and the ventricular rate was 26. The auricular complexes are all positive. *B*, Fifteen minutes later the auricular rate was 125 and the ventricular rate was 41. Both the T- and P-waves were markedly negative.

During the absence of the pulse, the electrocardiograms showed ventricular oscillations of a variable voltage from beat to beat (1 to 20 mm. high) irregular in their time relationship to each other (Fig. 2 *F*, *G*) with a duration of from 0.04 to 0.28 seconds each.

The auricular beats were not visible at this time. They reappeared irregularly as consciousness was restored when the ventricles assumed an almost regular rhythm and rate independent of their relation to the auricles (Fig. 2 *H*, *L*). The ventricular complexes were all slightly notched indicating probably that they arose from a different focus from that of the basic complexes.

Three minutes after these events, the patient began to sigh heavily. On examining her pulse it was found to be more rapid than previously and at times coupled; frequently three and four successive but weaker

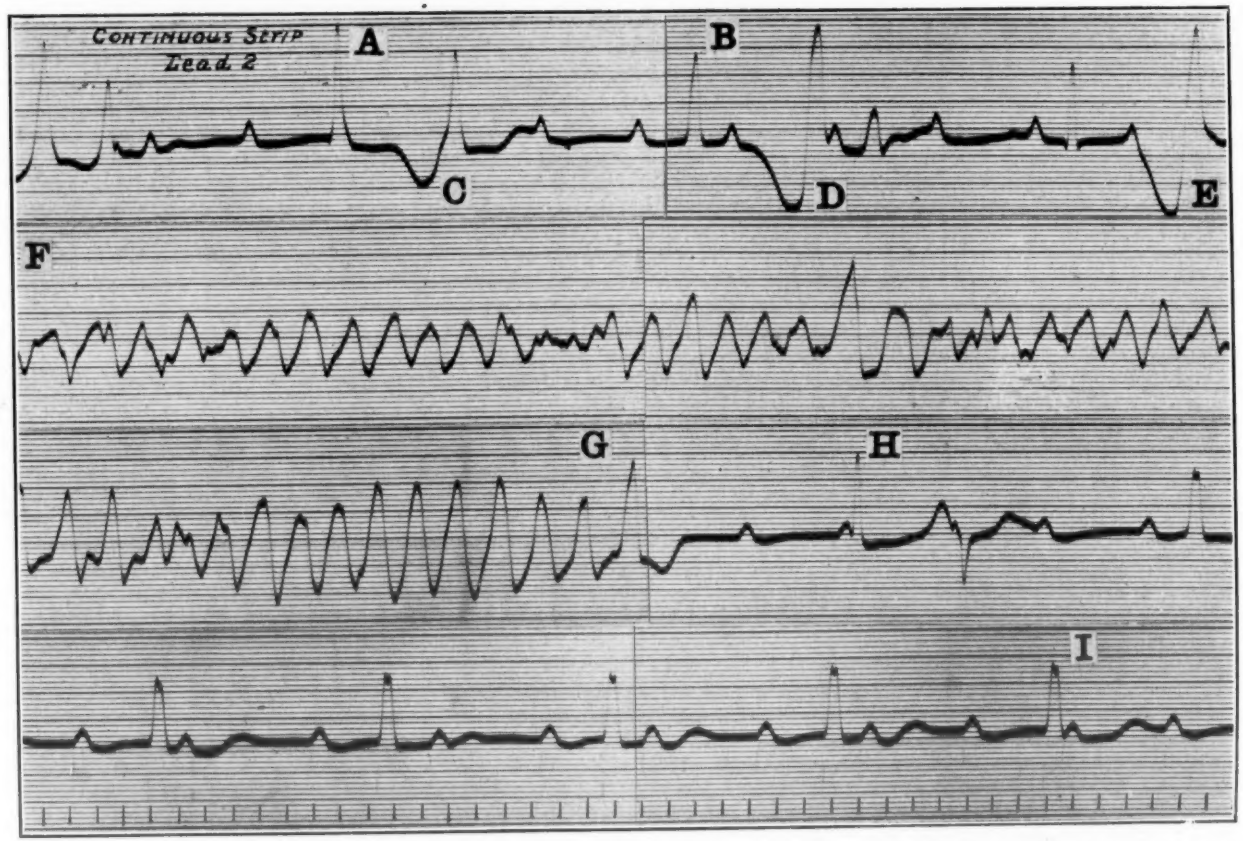

Fig. 2.—One and a half minutes after the injection of adrenalin. The basic ventricular complexes are large (*A*, *B*). The T-waves are now markedly negative and extremely large (*C*, *D*, *E*). There is bigeminal rhythm before a short period of ventricular fibrillation sets in (*F*, *G*).

beats could be felt, only the first two, however, being audible at the apex of the heart. The rate increased progressively and the electrocardiograms indicate this to be due to a recurrent grouping of ventricular oscillations following rapidly the basic ventricular complexes (Fig. 3 *A*, *B*, *C*) with an auricular rate which now averaged 140 beats per minute (Fig. 3).

After two minutes of this type of rhythm there again occurred an absence of the radial pulse which now lasted one minute and four seconds (Fig. 4).

The clinical syndrome this time resembled the characteristic Stokes-Adams seizures from which this patient suffered and which have been adequately described in another communication.[16]

The electrocardiograms again revealed a series of oscillations characteristic of ventricular fibrillation ending in spontaneous revival. Recovery of the basic rate was preceded by an idioventricular rhythm with retrograde auricular beats, most of which were superimposed upon the T-waves of the preceding ventricular complexes.

The ventricular rate, however, gradually increased to 41 beats per minute and the auricular rate to 125 before a period of ventricular tachysystole appeared fifteen minutes after the injection of adrenalin.

At this time the auricular complexes were at first negative (Fig. 1 *B*) but later they became positive as the ventricles assumed an irregular rate of 60 to 115 beats per minute, with impulses which appeared to be rising from various foci in the ventricles, although most of them were downward in character as compared with the complexes of the basic rhythm (Fig. 5).

Twenty minutes after the injection the ventricular rate returned to a level of 42 beats per minute (Fig. 6), and the auricles were beating at 125 beats before they suddenly began to fibrillate. The auricular fibrillation persisted for almost two hours following the use of adrenalin.

For the ensuing three hours there were no more recurrences of these irregularities described although the patient complained of persistent constriction of the chest for the rest of the day.

Subsequent observations revealed that short periods of ventricular fibrillation could be induced in her with 0.5 mg. of the drug given intramuscularly even in the presence of partial heart-block with a two-to-one rhythm.

However, at such times, the partial heart-block would be increased at first before there followed a gradual acceleration of both the auricular and ventricular rates leading eventually to the development of premature beats of the ventricles. These at first occurred singly, then in groups and ended finally in ventricular fibrillation. The longest period of ventricular fibrillation with syncope recorded in this patient as a result of adrenalin administration was one minute and four seconds, followed by spontaneous recovery.

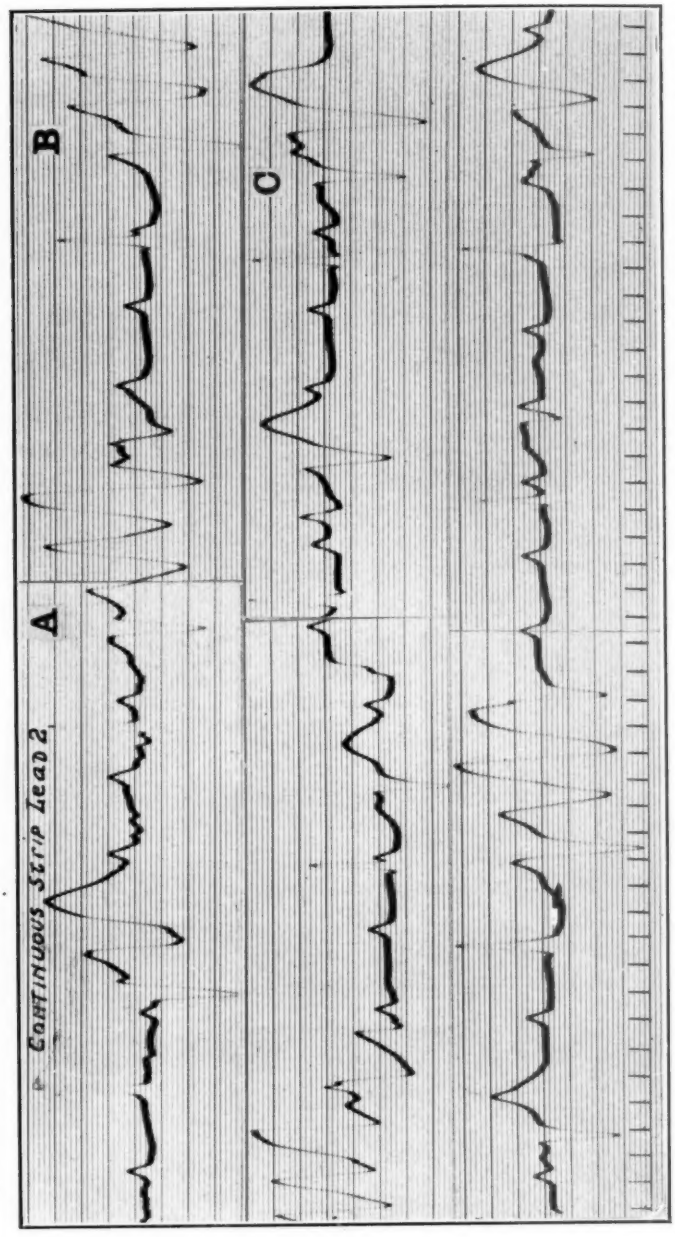

Fig. 3.—Three minutes after the injection of adrenalin. Recurrent groupings of aberrant ventricular oscillations (*A*, *B*, *D*). The auricular rate is now 140 beats per minute.

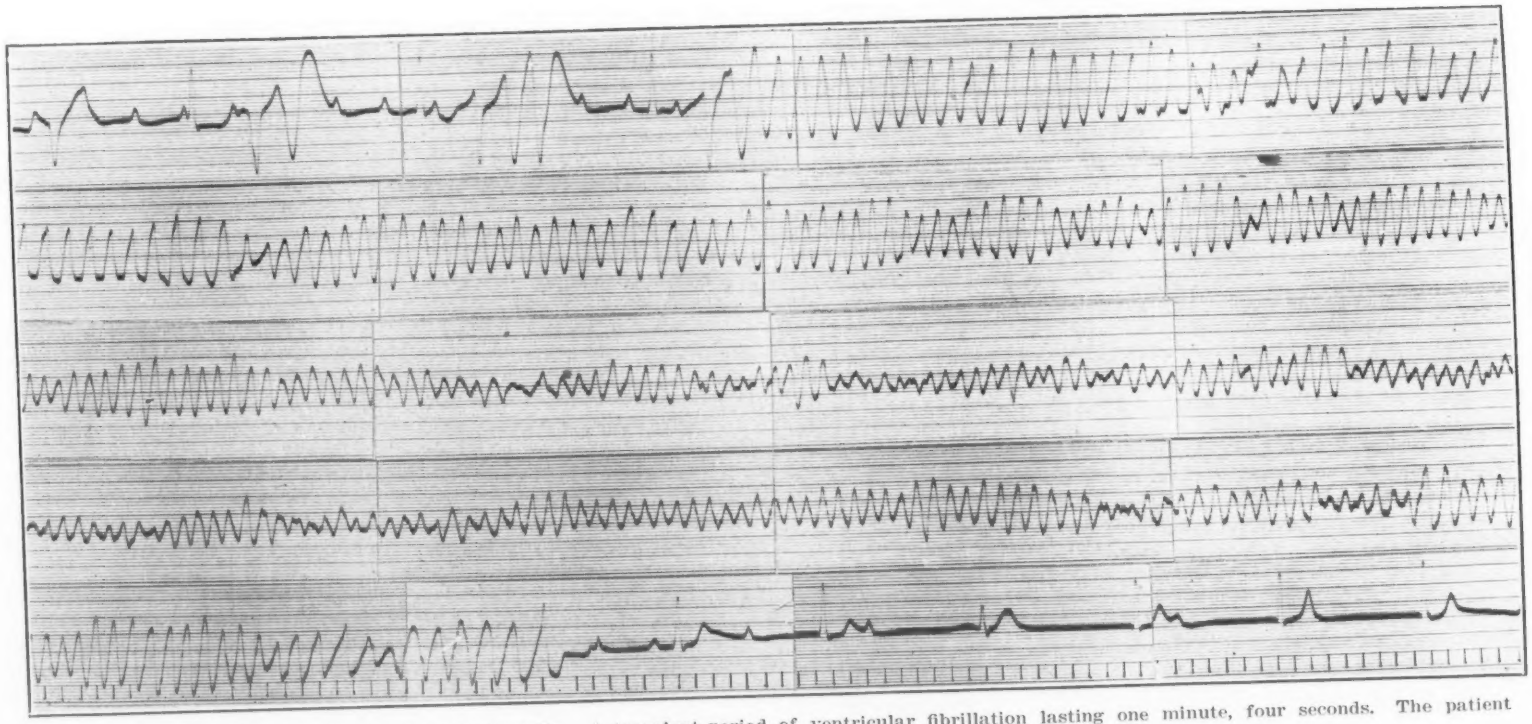

Fig. 4.—Five minutes after the injection of adrenalin. A transient period of ventricular fibrillation lasting one minute, four seconds. The patient was in syncope during this entire period.

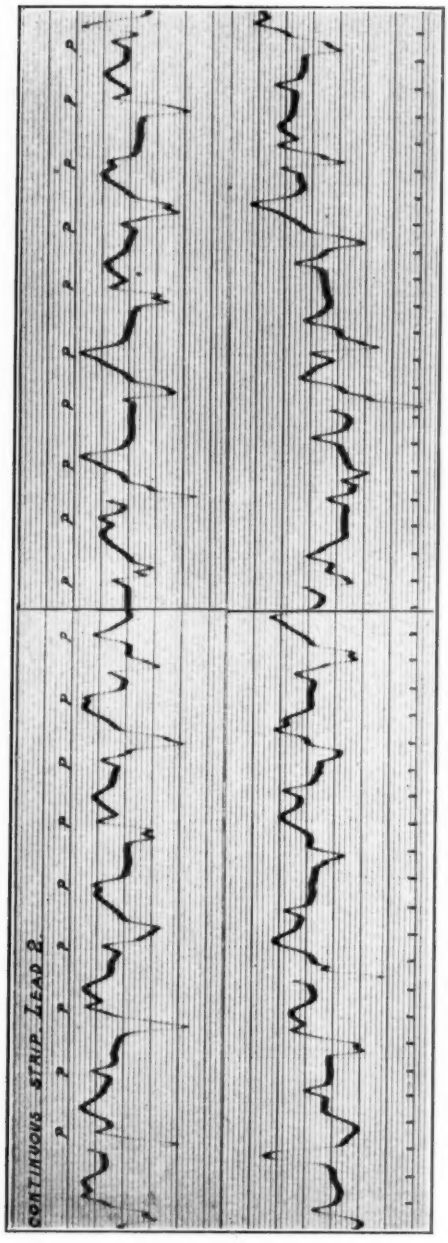

Fig. 5.—Fifteen minutes after the injection of adrenalin. This record was obtained thirty seconds after that in Fig. 1 *B*. The auricular rate is 115 and the auricular complexes are positive. The ventricular rate varies between 60 and 115 beats per minute.

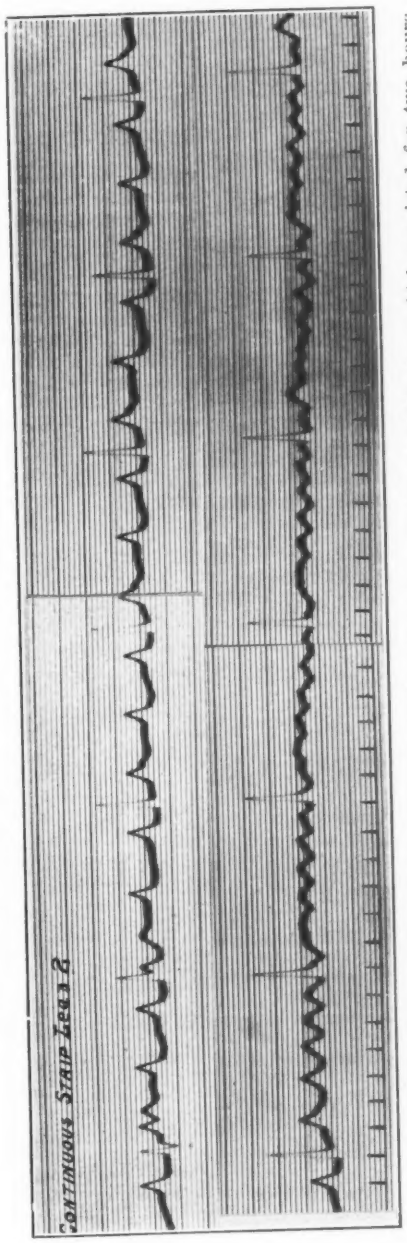

Fig. 6.—Twenty minutes after the injection of adrenalin. Transient auricular fibrillation, which persisted for two hours.

In the second patient, in whom ventricular fibrillation was the mechanism responsible for syncopal seizures, the intramuscular administration of 0.5 mg. of the drug resulted in a series of events similar to those described above but in a more severe form. Short periods of syncope due to ventricular fibrillation varying in duration from fifty seconds to one minute and fourteen seconds, alternated with periods of regular rhythm with a ventricular rate which averaged from 60 to 115 beats per minute. This sequence of events lasted for almost one hour before restoration of the basic rhythm took place. For the ensuing two hours there were recorded many premature beats of the ventricles, all of which, however, came through at the pulse.

On another occasion, the subcutaneous administration of a similar dose resulted only in an increase of the basic ventricular rate to a few beats per minute above the normal.

Finally, at a time when the patient had been in syncope for seven minutes and her respirations had ceased following a seizure of ventricular fibrillation, 1 mg. of adrenalin was injected directly into the heart. About one minute later, a strong beat at the pulse was seen to coincide with a flush of the face. Respirations were not re-established, however. For the next minute the ventricular rate increased to 115 beats per minute only to be followed again by a short run of ventricular fibrillation. Within the next thirteen minutes the heart rhythm, in the presence of loss of consciousness and absent respirations, consisted of a series of rapidly recurring periods of ventricular fibrillation alternating with a tachysystole of the ventricles, the end of which, however, could not be recorded graphically. Auricular fibrillation was never registered in this case.

DISCUSSION

The rational use of adrenalin in patients with auriculoventricular dissociation subject to Stokes-Adams seizures, depends upon an intimate knowledge of the mechanism responsible for the syncopal attacks.

It is important to appreciate that where a reduction in the ventricular rate or ventricular standstill is the cause of cerebral anemia resulting in syncope, adrenalin is the drug of choice. In such instances it may be used effectively in doses of 0.5 mg. to 1 mg. given intramuscularly. Judging from the electrocardiograms, it produces its effects on the rate and rhythm of the heart within one to three minutes following the injection. The results obtained are an increase in the idioventricular rate primarily through a stimulation of the idioventricular pacemaker. This increase is sometimes regular and at other times irregular. It reaches its maximum beneficial effects rapidly and lasts as long as four and one-half hours, when the rate slows down, at times to a level lower than that of the basic rhythm.

Even when the ventricular rate has already reached its basic level,

the repeated injections of adrenalin may prevent a slowing of the ventricular rate with resulting syncope. In patients with auriculoventricular dissociation the drug does this by maintaining a threshold of enhanced irritability of the auriculoventricular node. Excellent results have also been reported in such cases in which syncopal seizures have been prevented by the combined use of barium chloride[17] with adrenalin.[18] In cases refractory to adrenalin alone, the former drug increases the irritability of the idioventricular pacemaker and makes it more susceptible to the influence of adrenalin.

In patients with Stokes-Adams seizures due to ventricular fibrillation, however, the ventricles as well as the idioventricular pacemaker are already in a state of enhanced irritability. Therefore adrenalin is contraindicated both during the period of syncope and during the intervals between attacks. Our experience does not support the suggestion made by Dock[19] that small doses of the drug may cause ventricular fibrillation and large doses may arrest it.

It is possible that the small doses used by Lutembacher[10] where he observed "stoppage" of the heart and recorded a straight line in his polygraphic tracings also produced ventricular fibrillation, for both standstill of the ventricles and ventricular fibrillation give the same polygraphic records of the pulse during syncope, namely, a straight line indicating absent effectual contractions of the heart.

It should be apparent from these studies that the response to adrenalin as judged by the changes in the heart rhythm and rates of these patients is very variable from time to time. This variation is due neither to the drug nor to its mode of administration but probably to the state of irritability of the neuromuscular tissue of the heart. We have repeatedly observed marked systemic reactions, such as violent tremors, profuse diaphoresis and high rises in blood pressure, in the absence of any effects of the drug upon the cardiac rhythm.

Mention should be made here that our experience with the intramuscular injection of adrenalin in such patients has been limited to cases where the slowest ventricular rate during a period of syncope has been 6 beats per minute. It is obvious that absorption can take place in these cases as soon as the circulation is established, even by one effectual ventricular beat. It has been suggested that where complete standstill of the ventricles is responsible for syncope, adrenalin should be used intracardially, as has been done successfully by Levine and Matton[20] in one of their patients in whom standstill of the ventricles was recorded following a long period of ventricular fibrillation. However, in view of the fact that we have observed the effects of adrenalin on the heart during a period of ventricular fibrillation to be the same intramuscularly as it was intracardially, it is probable that the drug influences the heart rhythm and rate in another manner than through the circulating

blood stream, possibly through the sympathetic nervous system. Much more work will have to be carried out on this phase of adrenalin absorption before we may be certain of how it reaches the heart from the periphery when the circulation is at a standstill.

It may be questioned whether the electrocardiograms obtained in the two patients with syncopal seizures due to ventricular fibrillation following adrenalin were due to the drug, rather than to the natural course of events in such patients. For the records obtained during syncope following adrenalin resemble in every respect those obtained when syncope occurred spontaneously.[2] The progressive increase in the auricular rate during the premonitory period after adrenalin administration, the marked negativity of the P-waves following the fibrillatory period, the unusual tachysystole recorded before the restoration of the basic rhythm as well as the development of transient auricular fibrillation, all support the contention that the drug was responsible for these events. None of these phenomena was noted to have come spontaneously in this sequence, in a study of over one hundred recorded seizures of transient ventricular fibrillation in this patient.

SUMMARY AND CONCLUSIONS

Four patients who had complete auriculoventricular dissociation and who were subject to syncopal seizures received adrenalin in varying dosages. In two of the patients the syncopal attacks were due to a slowing of the ventricular rate, while in the other two the syncopal seizures were associated with transient periods of ventricular fibrillation.

The same dose of adrenalin was found to act variably at different times in the same patient when administered either subcutaneously or intramuscularly.

Adrenalin was found to increase both the auricular and the ventricular rates of the patients in whom the syncopal seizures were due to standstill of the ventricles. The increases in these rates were observed both preceding and during the Stokes-Adams attacks and were both regular and irregular in rhythm. The drug produced its effects primarily through a direct stimulation of the idioventricular pacemaker.

Adrenalin induced short periods of transient ventricular fibrillation with syncope in two patients in whom the Stokes-Adams attacks were found to be due to ventricular fibrillation. In one of these patients the drug also produced auricular fibrillation and a tachysystole of the ventricles which lasted on and off for several hours at one time.

In one patient with already established ventricular fibrillation the intracardiac injection of 1 mg. of the drug seemed to perpetuate the mechanism resulting in alternating periods of ventricular fibrillation with tachysystole lasting over thirteen minutes and ending in death.

As a therapeutic measure adrenalin is a life saving drug in patients in whom syncopal seizures are due to a slowing of the ventricular rate.

It is distinctly contraindicated in those in whom the attacks are the result of ventricular fibrillation, and its indiscriminate administration in such patients may result in death.

REFERENCES

1. Erlanger, J.: On the Physiology of Heart-Block in Mammals With Special Reference to the Causation of Stokes-Adams Disease. Part II. On the Physiology of Heart-Block in the Dog, J. Exper. Med. **8**: 8, 1906.
2. Schwartz, S. P.: Transient Ventricular Fibrillation. A Study of the Electrocardiograms Obtained in a Patient With Auriculoventricular Dissociation and Recurrent Syncopal Attacks, Arch. Int. Med. **49**: 282, 1932.
3. Cullis, W., and Tribe, M. E: Distribution of the Nerves of the Heart, J. Physiol. **46**: 141, 1913.
4. Van Egmond, A. A. J.: Ueber die Wirkung einiger Arzneimittel beim vollstandingen Herzblock, Arch. f. d. ges. Physiol. **154**: 39, 1913.
5. Routier, D.: Action de l'Adrenaline sur le coeur bloque du chien, C. R. Soc. de Biol. **78**: 375, 1915.
6. Hardoy, P. J., and Houssay, B. A.: Note sur l'Action de l'Adrenaline dans la Dissociation Auriculo-Ventriculaire, J. de physiol. et de path. Gén. **17**: 605, 1917-1918.
7. Danielopolu, D, and Danulescu, V.: Action de l'Adrenaline dans la bloquage complète du coeur, C. R. Soc. de Biol. **79**: 861, 1916.
8. Danielopolu, D., and Danulescu, V.: Action de l'Adrenaline dans la Dissociation Auriculo-Ventriculaire incomplète, C. R. Soc. de Biol. **79**: 105, 1916.
9. Arrilaga, F. C.: Abstract, Arch. d. mal. du coeur **13**: 370, 1920.
10. Lutembacher, R.: Action de l'Adrenaline sur le coeur en état de Dissociation Auriculo-Ventriculaire, Arch. d. mal. du coeur **13**: 345, 1920.
11. Strissower, R.: Pharmacalogische Beinflussung des Pulses bei einem Fall von Herzblock, Wein. klin. Wchnschr. **33**: 269, 1920.
12. Phear, A. G., and Parkinson, J.: Adrenalin in the Stokes-Adams Syndrome, Lancet **202**: 933, 1922.
13. Feil, H.: The Use of Epinephrin in the Stokes-Adams Syndrome, J. A. M. A. **80**: 26, 1923.
14. Parkinson, J., and Bain, C. W. C.: The Adrenalin Treatment of Stokes-Adams Disease, Lancet **207**: 311, 1924.
15. Korns, H. M., and Christie, C. D.: Note on the Use of Epinephrin in Heart-Block, J. A. M. A. **79**: 1606, 1922.
16. Schwartz, S. P., and Jezer, A.: Transient Ventricular Fibrillation. The Clinical and Electrocardiographic Manifestation of the Syncopal Seizures in a Patient With Auriculoventricular Dissociation, Arch. Int. Med. (In press.)
17. Cohen, A. E., and Levine, S. A.: Beneficial Results of Barium Chloride on Adams-Stokes Disease, Arch. Int. Med. **36**: 1, 1925.
18. Price, F. W., and Nisse, S. B.: The Treatment of Adams-Stokes Syndrome Due to Auriculoventricular Block, Am. Heart J. **5**: 197, 1929.
19. Dock, W.: Transitory Ventricular Fibrillation as a Cause of Syncope and Its Prevention by Quinidine Sulphate, Am. Heart J. **4**: 709, 1929.
20. Levine, S. A., and Matton, M.: Observations on a Case of Adams-Stokes Syndrome, Showing Ventricular Fibrillation and Asystole Lasting Five Minutes, With Recovery Following the Intracardiac Injection of Adrenalin. Heart, **12**: 271, 1925.

AURICULOVENTRICULAR NODAL PAROXYSMAL TACHYCARDIA AND AURICULAR FLUTTER. CASE REPORT*

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THE purpose of this paper is to present a very unusual example of cardiac arrhythmia observed in a patient admitted to the Worcester City Hospital because of an acute bronchopneumonia. The electrocardiographic diagnosis was auriculoventricular nodal paroxysmal tachycardia, interrupted at varying intervals by auricular flutter with varying degrees of heart-block. A-V nodal paroxysmal tachycardia is of itself a rather rare form of arrhythmia, having occurred only four times in a series of 10,000 patients (0.04 per cent) whose electrocardiograms were recorded at the Massachusetts General Hospital over a period of sixteen years (1914-1930).[1] At the Mayo Clinic over a period of nine years (1914-1923), 102 cases of paroxysmal tachycardia were electrocardiographed. Only three of these had an R-P interval as demonstrated in the case to be discussed.[2] However, the case which we are presenting has its claim to distinction in the fact that the nodal rhythm is interrupted by short runs of flutter, with varying block. No exactly parallel case has been observed in a careful search of the literature. P. D. White describes the course of a patient who had auricular flutter which digitalis converted to auricular fibrillation and then to a rhythm which had its origin in the A-V junctional tissues.[3] W. E. Hume, by means of the polygraph, was able to demonstrate, in two cases of diphtheria, the transition of an A-V nodal rhythm (not paroxysmal tachycardia) into auricular flutter, terminating in death for the patients.[4] Two cases which to some extent approach the case at hand have been reported by Géraudel. These patients were observed over a period of from two to four years. Tracings at certain periods showed rhythm simulating either a nodal tachycardia or an auricular tachycardia. At other times flutter with 2-1 block was found and occasionally a third phase was recorded in which there would be groups of two, three, and four ventricular complexes similar to those found in the period of tachycardia—each with its own auricular or nodal origin. Then would come two auricular contractions to one of the ventricular contractions (flutter with 2-1 block) seemingly linking up the two phases. In view of these findings the author drew the conclusions that paroxysmal tachycardia did not exist at all but was simulated by a flutter with a 1-1 response.[5] There can be no question of the distinction of the two rhythms in the case at hand (i.e., A-V nodal paroxysmal tachycardia and auricular flutter).

*From the Department of Cardiology of the Worcester City Hospital.

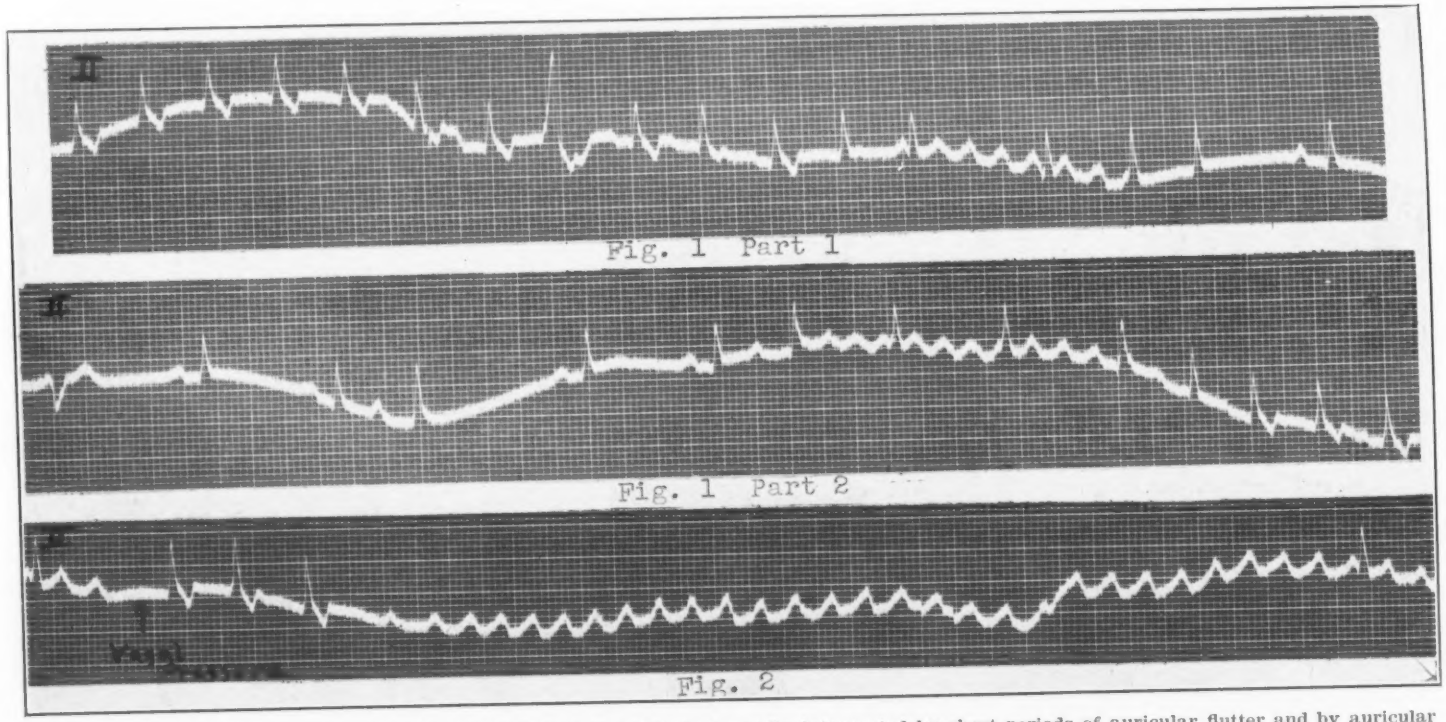

Fig. 1.—Electrocardiogram (Lead II) showing A-V nodal tachycardia interrupted by short periods of auricular flutter and by auricular and ventricular premature beats (see text). Part 2 is a continuation of Part 1.

Fig. 2.—Effect of vagal pressure, applied at the end of a period of auricular flutter and during a short run of beats of A-V nodal tachycardia, showing 29-1 heart-block in a succeeding interval of auricular flutter.

CASE REPORT

History.—The patient, a forty-three-year-old married man, entered the Hospital on September 15, 1931, having been sick five days at home. He complained chiefly of pain in the left upper chest. Five days previously he was playing with his dog when he was seized with a sharp pain over the tops of both shoulders. There

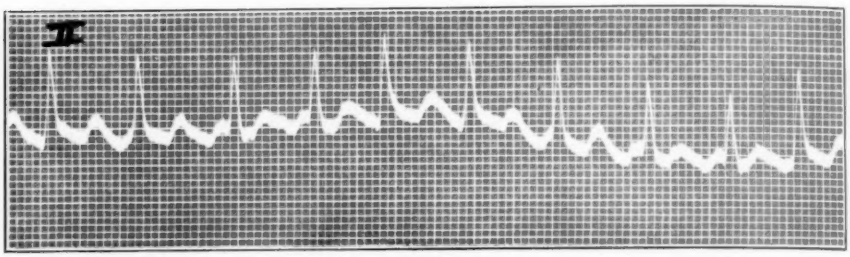

Fig. 3.—Electrocardiogram after quinidine sulphate showing auricular flutter with two-to-one block.

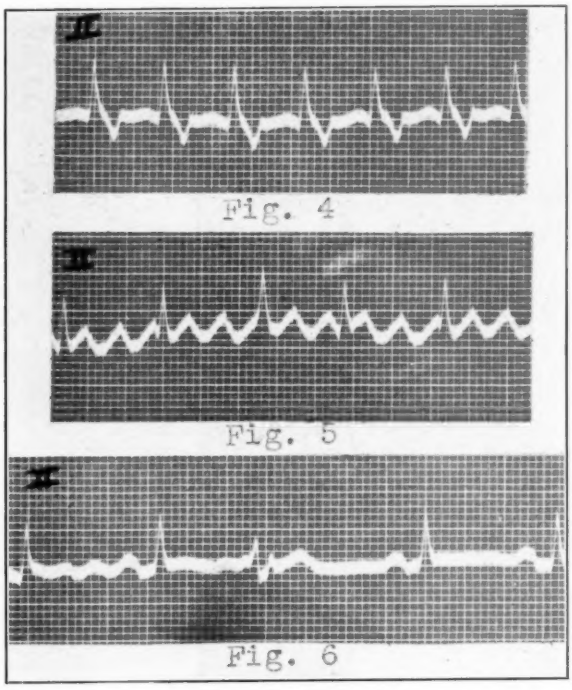

Fig. 4.—A-V nodal paroxysmal tachycardia before atropine sulphate.
Fig. 5.—Auricular flutter with two-to-one and three-to-one block, one minute after atropine sulphate.
Fig. 6.—Return to normal rhythm, four minutes after atropine sulphate.

were no chills, cough, or pain on respiration. This pain lasted three to four days and was not severe enough to make him go to bed. The following day he felt a tightness in the left axillary line at the level of his heart and had some difficulty in breathing. Two days before admission to the hospital he commenced to cough a bit and felt feverish.

Family History.—Irrelevant.

Past History.—He had rheumatic fever at fifteen years of age, at which time he was laid up for one year. Since then he has never had dyspnea, edema, precordial pain or distress, or any symptoms suggestive of cardiac failure. He has, however, as long as he can remember, been conscious of marked variations in his pulse rate. Particularly after exercise, such as golf, is he conscious of a very rapid pounding of his heart. This palpitation may suddenly stop of its own accord; at other times he is able to terminate the attack by holding his breath or by bending forward. Aside from this abnormality the patient has always been well.

Physical Examination.—A middle-aged man with flushed face sitting up in bed breathing rapidly. His temperature was 101°, pulse 134 and regular, respirations 40. Examination of the lungs showed dullness to percussion at both bases with coarse râles extending up to the angles of the scapulae. These signs were more extensive on the left than on the right. No points of consolidation were made out. The heart was thought to be enlarged to percussion. The sounds were of good quality.

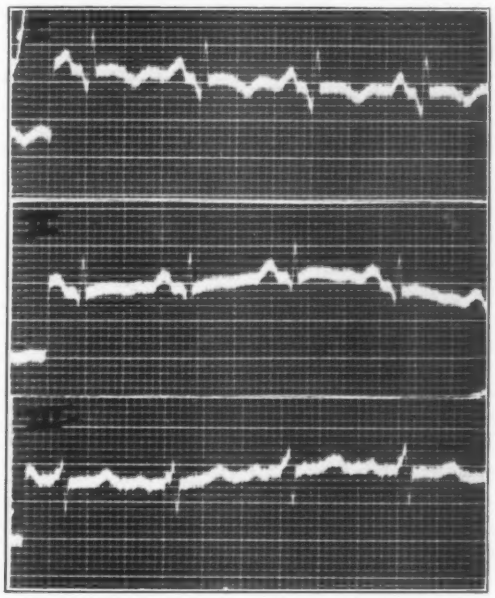

Fig. 7.—Showing patient's normal rhythm at the follow-up visit.

No murmurs were heard. The blood pressure was 140 mm. systolic and 100 diastolic. Physical examination was otherwise not abnormal.

Laboratory Findings.—The urine examinations were normal. The white blood cell count was 18,000. The sputum contained group IV Pneumococcus. The basal metabolism was not elevated. The Wassermann reaction was not recorded.

Progress.—The temperature and respirations gradually fell to normal over a period of six days. For the next few days the patient's pulse rate was quite variable. Sometimes it would be 130 to 140; at other times it would be 70; sometimes it would be irregular; other times regular. The patient insisted if he were allowed to get up his heart would return to its normal condition. Consequently on the seventh day following the drop in temperature he was allowed up. As he had predicted, his pulse became quite regular with only occasional paroxysms of tachycardia. Although the diagnosis in this case was acute bronchopneumonia the patient was given digitalis perhaps rather empirically. With the fall in temperature on the sixth day digitalis was omitted. He had received 19½ grains.

There had been no other medication of note. He was discharged on the fourteenth day.

The patient came to the hospital November 23, 1931 (eight weeks after his discharge) for a follow-up visit. He stated that he was feeling very well indeed. At night he might have an occasional attack of palpitation just after getting into bed. The attack would last only a few minutes and seemed never to occur during the daytime. Examination of the heart revealed no further abnormalities than found at the previous examination. An electrocardiogram was taken, the three leads of which are to be seen in Fig. 7.

ELECTROCARDIOGRAPHIC OBSERVATIONS

Our observations on the patient's cardiac abnormalities were made from the time his temperature fell to normal on the sixth day. The first electrocardiogram was taken on the sixth day. (Fig. 1. Part 2 is a continuation of Part 1.*) The initial rhythm is a tachycardia (rate 160) with an impulse arising at or near the A-V node (i.e., an A-V nodal tachycardia). The wave of origin of the impulse is incorporated in the QRS complex and there is a retrogression of the impulse into the auricle to produce an inverted P-wave directly following the QRS, thus producing an R-P interval. This type of tachycardia is interrupted at one point by a paroxysm of auricular flutter first with a 4-1 block and then a 3-1 block. The next complex is an escaped ventricular beat. Following this is a contraction whose origin is supraventricular, though not at the usual site in the S-A node. (Compare normal rhythm in Fig. 7.) Next there appears a premature ventricular beat following which the heart returns to its normal S-A rhythm, but for two contractions only. A premature auricular beat intercedes, coming from an ectopic focus. Shortly later there appears another paroxysm of auricular flutter which seems to be initiated by a premature auricular beat. First there is a 3-1 block and then 4-1 and 3-1 block. Finally the heart reverts to a typical A-V nodal paroxysmal tachycardia.

Effect of Vagal Pressure.—Pressure on the right carotid sheath was applied at a time when the heart was responding to the nodal focus (Fig. 2). A condition of ventricular standstill was produced which lasted for a period of 6.2 seconds. During this period there was an isolated P-wave followed by a regular action of the auricle at a rate of about 300 per minute. This situation did not bother the patient subjectively. He stated that he felt dizzy. He did not lose consciousness. This was the only time that we were able to produce such a vagal effect.

Effect of Quinidine Sulphate.—After taking the above electrocardiograms, twelve grains of quinidine sulphate were given, with no change in the rhythm. Fifteen grains were given on each of the next two days. On the third day the rate was found to be 150 and apparently regular. The patient was then given twenty-one grains of quinidine, at which point he complained of ringing in the ears. He was conscious

*Lead II is used in the figures except where otherwise indicated.

(more so than usual) of his heart's beating and complained that he had felt worse since the quinidine treatment had been instituted. A tracing was then taken (Fig. 3) showing a slight irregularity of incidence of the ventricular contractions at a rate of 150 to the minute. A flutter with a 2-1 block is the dominant rhythm and no instance of the A-V nodal rhythm was found. Deep breathing did not affect this tracing. Vagal pressure served temporarily to increase the block to 4-1 and then to 3-1. We were unable to obtain a normal sinus rhythm after moderate doses of quinidine sulphate.

Effect of Atropine Sulphate.—On the following day the electrocardiogram showed a return to A-V nodal paroxysmal tachycardia (Fig. 4). Atropine sulphate 1/100 grain was injected subcutaneously. In one minute there was a flutter with block changing from 2-1 to 3-1 (Fig. 5). This persisted for three more minutes when the heart returned to a normal sinus rhythm (Fig. 6) with an occasional premature nodal beat at a rate of 100. After six minutes the normal rhythm was displaced by a flutter with varying block. Forced expiration would sometimes convert the flutter to a normal rhythm.

Atropine was given, grains 1/100 by mouth, every four hours for forty-eight hours and then reduced to grains 1/150 every four hours and a tracing taken on the third day following. Considerable irregularity of the heart beat was still present. The cardiogram showed a tendency to coupling with a normal sinus beat followed by a premature auricular beat though at times the rhythm became normal or would change to the nodal tachycardia.

DISCUSSION

This patient evidently had a very irritable heart. The rôle of the pacemaker is at times usurped by a focus of rapid impulse formation at or near the A-V node. At other times this nodal focus is supplanted by a focus higher up in the auricle where there is a regular circus movement forming impulses twice as fast as the nodal focus (the interval between ventricular beats in the periods of tachycardia, representing the intervals between nodal impulses, is twice as long as the interval between P-waves in the stages of flutter). A flutter with 2-1 and increasing block then develops. Apparently there are two areas of abnormal impulse formation, the one in the A-V node causing a paroxysmal tachycardia, the other focus occurring higher up and instituting a state of flutter. First one area comes into control, then is gradually displaced by the other area. A very disordered heart beat results.

Vagal pressure may exert a greater effect in A-V rhythm than in S-A rhythm.[6] Vagal stimulation in this case produced a 29-1 block, the auricle contracting twenty-nine times in response to the upper

focus. The auricular rate is the same as at the periods of flutter scattered through the runs of nodal tachycardia.

The S-A node though greatly depressed has not lost its function as evidenced by the occasional instances of normal sinus rhythm. Atropine by its paralyzing action on the vagus nerve endings seems to remove this inhibition, allowing the S-A node to resume its normal rôle for short periods of time. However, its reign is apt to be terminated at any moment by the return of control by the ectopic foci.

SUMMARY

A case of peculiar cardiac arrhythmia is reported in a man forty-three years old, and electrocardiograms showing the mechanism of the disordered heart beat are presented. The dominant rhythm is an auriculoventricular nodal paroxysmal tachycardia which at varying intervals becomes displaced by an auricular flutter with changing block. The effects of vagal pressure, quinidine sulphate, and atropine sulphate on this disordered rhythm are demonstrated.

The author of this paper wishes to acknowledge the kind assistance of Dr. P. D. White of Boston in reporting this case, and the interest of Dr. G. M. Albee of Worcester whose patient it is who forms the subject matter for this report.

REFERENCES

1. White, P. D., and Sprague, H. B.: Electrocardiography of 10,000 Patients at the Massachusetts General Hospital from 1914 to 1931, Kasan M. J., p. 381, 1931.
2. Willius, F. A., and Barnes, A. R.: Paroxysmal Tachycardia With Special Reference to Progress, Boston Med. and Surg. J. **191**: 666, 1924.
3. White, P. D.: A-V Rhythm Following Auricular Flutter, Arch. Int. Med. **16**: 517, 1915.
4. Hume, W. E.: A Polygraphic Study of Four Cases of Diphtheria With a Pathological Examination of Three Cases, Heart **5**: 25, 1913.
5. Géraudel, E.: Paroxysmal Tachycardia and Flutter, Arch. des Mal. du Coeur **21**: 273, 1928.
6. Lewis, Thomas: Effect of Vagal Stimulation on A-V Rhythm, Heart **5**: 247, 1914.

Department of Clinical Reports

ACUTE PULMONARY EDEMA

Report of a Case With Autopsy*

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THIS term was first used by Huchard[1] in 1897 to describe the case of a patient suffering from a cardiac condition complicated by sudden and severe attacks of edema of the lungs. Numerous writers since then have written of this condition under various captions as cardiac asthma, paroxysmal acute dyspnea and paroxysmal dyspnea of hypertension. Palmer and White[2] in an excellent summary described it as a "condition of paroxysmal acute dyspnea, generally occurring at night, but sometimes following exertion, lasting from minutes to hours and accompanied by a sense of suffocation, by wheezing and often by cough with frothy sputum which may or may not be bloody and which is due fundamentally to serious heart disease, especially involving the left ventricle, the attack being characteristically relieved by morphine."

Just as the terminology describing these attacks has differed, so has the exact nature of the attack and the causation been subject to various interpretations. The earliest and most outstanding experimental work was done by William Henry Welch[3] in 1878, in which he injured the left ventricle of rabbits producing a pulmonary edema. According to Welch, the condition is one in which "A disproportion exists between the working power of the left ventricle and of the right ventricle of such a character that, the resistance remaining the same, the left heart is unable to expel in a unit of time, the same quantity of blood as the right heart." Cohnheim at once supported this theory but Sahli and Grossman criticized it though they offered no experimental evidence to refute it, nor any equally satisfactory explanation. Vaquez considers several possible causes, the mechanical, the angioneurotic, the toxic and the mixed forms. He favors apparently the idea that most of the attacks can be laid directly to failure of the left ventricle. Pratt,[5] in a review of thirty-nine cases of cardiac asthma, feels that a peripheral vasomotor disturbance is a strong factor in many cases, and also suggests that there may be an element of bronchial spasm present. The opinion of Palmer and White is that left ventricular strain and failure cause, with increased blood flow, a stasis of blood in the pulmonary circulation, the right ventricle sending too much blood for the left ventricle to take care of. Practically all writers agree that the one most important associated finding in all cases of acute pulmonary edema is a

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marked coronary sclerosis. This interferes with coronary flow, causes myocardial ischemia and failure on the part of the ventricle to maintain a required output.

This paper does not concern itself with the pulmonary edema of cardiac decompensation accompanying valvular disease, nor do we refer to the gradually developing edema seen in the failing heart of myocarditis either of the fibrous or infectious type. Edema of the lungs occurring in allergic cases, chronic infections, bronchitis and so-called angioneurotic conditions differs clinically and symptomatically from the acute or paroxysmal type. The condition is fundamentally the result of sudden left ventricular overstrain plus acute myocardial failure with all the concomitant symptoms of complete collapse. The ashen pallor, urgent dyspnea, cold surface, clammy sweat, rapid pulse, fall of tension and hopeless expression of the patient, create a singular picture seen in no other form of pulmonary edema. Recovery from the seizure is equally striking. The patient's sensation of relief from overpowering oppression, the cessation of sweating, the return of body warmth, are soon followed by a lessening of the tachycardia, a fuller pulse, a return of color and a gradual vanishing of the dyspnea and signs of pulmonary edema. The attack may be very mild, so slight that only the patient senses a feeling of difficult breathing and perhaps some alarm. If the seizure progresses it may develop with aggravating intensity and result in death in a few minutes. The entire episode may be over in a few minutes, or it may progress with alarming intensity, reach its climax, slowly subside and be completely over in an hour.

After repeated attacks, the period of recovery is prolonged. However, when all the features have vanished, no objective or physical signs remain or even suggest that the patient has passed through a critical seizure. Though this condition is not infrequent in practice, the opportunity for prolonged observation and for intensive clinical study of a case of acute pulmonary edema is not common.

In the report given below not only was the patient seen prior to his initial attack but in each subsequent seizure it was possible to make clinical and electrocardiographic studies, observe the factors that precipitated each attack and note the effects of various forms of medication. Supplementing the prolonged observation of this case, the autopsy findings revealed definite changes that supported the explanation of left ventricular myocardial damage.

CASE HISTORY

Male, aged sixty-two years, married, merchant, came for physical examination for the first time in 1916. He felt perfectly well but expressed the desire to have regular and complete examinations. Noteworthy in his family history were the facts that his mother, aunt and uncle had died of diabetes and that his father and brother had died of coronary disease. One sister was living and well. There was nothing of importance in his past or personal history. There was no history of rheumatism, and syphilis was denied. At the time of the initial examination,

a mild hypertension, 150 systolic and 90 diastolic, was recorded. There was no evidence of cardiac enlargement. On subsequent occasions during the next six years the blood pressure was recorded at various heights, the maximum ever found was 184 systolic and 110 diastolic. Several times traces of albumin and a rare hyaline cast were reported in the urine.

In 1922 the patient complained for the first time of pain in his chest radiating into the left arm, made worse by exertion and accompanied by fear of possible consequences. Whether the angor animi was spontaneous or due to the patient's knowledge of symptoms of the disease, could never be determined. During the next few years the increasing frequency and severity left no doubt of the fact that these were attacks of stenocardia on the basis of a coronary sclerosis. With this in mind general directions concerning restrictions in activity, mental strain, diet and habits together with instructions with regard to the use of nitroglycerine, were given. In 1925, he had his first paroxysm of acute pulmonary edema. It came on with exercise; it was relieved by one-fourth grain of morphine. Two years elapsed before he had a return of a similar condition though in the meantime he continued to have anginal attacks of varying intensity. He carried nitroglycerine constantly and used it liberally with benefit. In 1927 he began having attacks of pulmonary edema more frequently so that between that time and his death in October, 1930, he was seen in some attacks of great severity.

Physical examination revealed a small man weighing 65 kg. His skin was smooth and dry and his musculature was poorly developed. There was slight enlargement of the heart to the left and downward. The sounds were clear; the aortic second was moderately accentuated. There was normal vesicular breathing throughout the lungs. The edge of the liver could be felt on deep breathing. The abdomen was otherwise normal. Though his blood pressure maintained a higher level up to 1925, after that it gradually fell, averaging during the last five years 150 systolic and 100 diastolic. The blood count was normal. The Wassermann test was negative. X-ray films revealed a slight enlargement of the left ventricle. There was no change in appearance of the aortic shadow. The lung fields were clear. There was moderate hilus infiltration. The phrenocosto angles were clear. Electrocardiograms revealed changes indicating marked disease of the coronary arteries.

Course of the Disease.—Although the patient suffered almost daily attacks of stenocardia from 1927 up to his fatal seizure in 1930, he nevertheless remained active in business and continued with moderate exercise. He played golf in pleasant weather and spent much leisure time at cards. Neither moderate work nor recreation were harmful. Physical and emotional strain precipitated attacks. Overeating and excessive smoking had a similar effect. Yet the patient knew his limitations and managed to live within them. He took a philosophic view of his condition and tried to avoid those forms of excitement, overactivity, and overindulgence that would precipitate stenocardia. However, he chose moderate freedom to excessive restraint, preferring to control the pain with nitroglycerine. This was accomplished effectively with 1/100 grain of nitroglycerine which the patient repeated sometimes at fifteen-minute intervals.

During the last three years of his life, attacks of acute pulmonary edema also became increasingly frequent. The attacks of edema were not necessarily associated with stenocardia. At the same time attacks of angina of varying intensity frequently developed without any evidence of either edema or dyspnea. In fact, from this case, it is evident to us that severe attacks of stenocardia can occur even in the presence of a badly damaged left ventricle without producing acute pulmonary edema. The fatal attack was precipitated by intense emotional excitement. In this last attack he was sitting in his chair speaking with friends. He was under decided emotional stress when without warning he complained of

distress in his chest, developed rapid labored asthmatic breathing, grew ashen pale and died immediately.

During an attack, the heart sounds were usually obscured by coarse râles heard everywhere in the chest. His extremities were cold, his skin slightly cyanotic and an expression of extreme anguish developed. He was usually propped up in a semisitting position, hardly able to speak and struggling for every breath. Cardiac dilatation could not be demonstrated by physical or fluoroscopic examination; and there was never any elevation of blood pressure. Occasionally there would be a ten or fifteen point fall in both the systolic and diastolic levels.

For the relief of these attacks many different substances such as amyl nitrate, nitroglycerine, adrenalin, caffeine sodium benzoate and digitalis were tried, but were always found ineffective. Morphine in doses of 1/6 to 1/2 grains was invaluable and often within a few minutes would bring such complete relief that all râles would entirely disappear from the chest and the patient would lie down with comfort. Bed rest for a few days following and digitalis between the at-

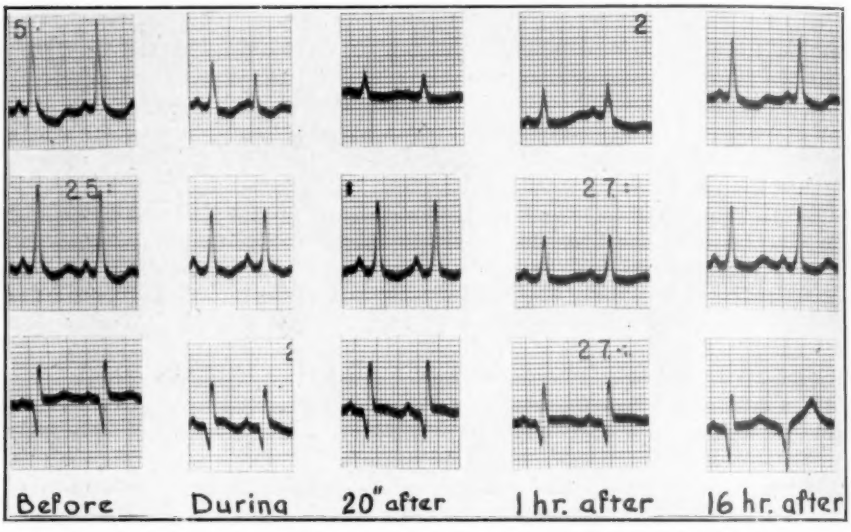

Fig. 1.—Electrocardiographic studies before, during, and after a typical severe attack. Note the marked fall of amplitude almost entirely in the left axis.

tacks seemed effective in preventing their occurrence. Unfortunately, it was impossible to restrict this patient as fully as was desirable. He preferred death to complete invalidism and refused many of the essential physical and emotional restrictions.

Electrocardiographic studies were made during a typical attack and the findings will be noted in Fig. 1. In the tracing taken one week before this attack, the marked S-T change, the diphasic T_1 and T_2, and the slightly increased intraventricular conduction will be noted as indicative of marked coronary disease. At the onset of the attack there is apparent a fall of voltage of the QRS, and increased rate and ventricular extrasystoles. As the attack progresses the height of the R-wave falls very perceptibly, chiefly in Lead I and even after sixteen hours have elapsed, there is evident considerable left ventricular weakening as judged by the fall in height of R_1 and R_2.

Autopsy revealed nothing of importance except in the cardiovascular system. The heart weighed 575 grams. On the posterior wall of the left ventricle, a flabby,

softened, pale area 4.5 by 6 cm. was seen. On sectioning, this proved to be an area of old healed infarction. The wall at this point was only 0.5 cm. in thickness, whereas the wall of the remainder of the left ventricle was 2.5 cm. in thickness. The valves of the heart were normal. The coronary arteries were markedly sclerosed throughout. The wall of the right ventricle appeared quite normal and measured 0.6 cm. in thickness. Fig. 2 shows the large fibrotic area in the left ventricle. There were moderate arteriosclerotic changes in the aorta and in all the smaller arteries throughout the body. The lungs were negative. The kidneys showed a moderate degree of vascular change. It was evident that this marked weakening of the wall of the left ventricle was the basis for the attacks of acute pulmonary edema.

Physical or emotional strain, by increasing the heart rate or elevating the blood pressure, threw an additional load upon the ventricles, already subject to diminished coronary flow. As a result there developed an excessive strain of the damaged and already deficient left ventricle, causing that chamber of the

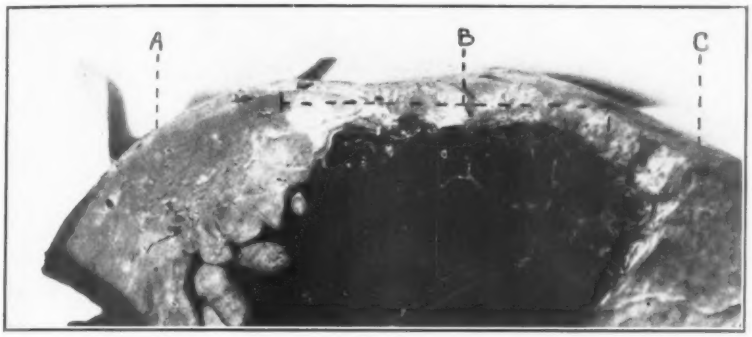

Fig. 2.—Section of heart showing thin, fibrotic area of healed infarct. (*A*) Lateral wall of hypertrophied left ventricle. (*B*) Healed infarct in posterior wall of left ventricle. (*C*) Region of ventricular septum.

heart to lag behind the right ventricle. Arterial output fell behind, pulmonary stasis quickly formed; engorgement and edema resulted. This is in accord with the theory first advanced by Welch and now generally accepted, namely, that the most frequent cause of attacks of acute pulmonary edema is left ventricular failure with ensuing disproportion between right and left chambers.

SUMMARY

A case is presented which offers detailed clinical and electrocardiographic study of the nature and causation of attacks of acute pulmonary edema. Autopsy findings substantiate the clinical diagnosis and are further verification of the accepted theory of the cause of this syndrome.

REFERENCES

1. Huchard, M. H.: L'Oedeme aigü du Poumon, Bull. Acad. de Med. **37**: 492, 1897.
2. Palmer, R. S., and White, P. D.: The Clinical Significance of Cardiac Asthma, J. A. M. A. **92**: 431, 1929.
3. Welch, William Henry: Theory of Pulmonary Edema. Papers and addresses by William Henry Welch, Johns Hopkins Press, p. 36, 1920.
4. Vaquez, Henri: Diseases of the Heart, Philadelphia, 1925, W. B. Saunders Co., p. 637.
5. Pratt, J. H.: Cardiac Asthma, J. A. M. A. **87**: 809, 1926.

BUNDLE-BRANCH BLOCK WITH PERIODS OF NORMAL INTRAVENTRICULAR CONDUCTION: REPORT OF AN UNUSUAL CASE*

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SEVERE grades of delayed intraventricular conduction are usually permanent and are commonly regarded as indicative of pathological changes of the myocardium. It is not generally recognized that such conduction disturbances may be primarily functional in nature and transitory in occurrence. Herrmann and Ashman,[1] in a recent review of this subject, collected ten cases from the literature in which the intraventricular conduction time was found to vary at different periods of observation. They report in detail eight instances of their own. Three of these were remarkable in that a complete change from bundle-branch block to normal intraventricular conduction occurred during the period of a single cardiac cycle in response to simple maneuvers (breath holding, slight exercise). Wenckebach and Winterberg[2] published tracings obtained from a girl eleven years of age which usually showed partial A-V block with a P-R interval of 0.22, together with altered ventricular complexes which they regarded as indicative of right bundle-branch block. Slight exercise was sufficient to induce a 2:1 A-V block and to cause complete disappearance of the intraventricular conduction delay. At autopsy there was slight structural alteration of the conduction system hardly sufficient in degree to account for the pronounced changes observed in the electrocardiogram. This observation is of particular interest because it indicates that profound intraventricular conduction disturbances may be primarily of a functional nature. It is of course evident that the prognosis in such instances might be favorable.

We wish to describe a patient without cardiac symptoms in whom there occurred abrupt changes from bundle-branch block to normal intraventricular conduction, both spontaneously in combination with transitory 2:1 A-V block, and in the absence of such block, as the result of indirect vagal stimulation.

CASE REPORT

The patient was an obese white man sixty-six years of age who presented himself for general physical examination. He had no complaints. His hereditary background was good; his parents had lived to old age. He had had uncomplicated scarlet fever at twenty-two years of age, and gonorrhea at twenty. Syphilis was denied. There was no history of rheumatic fever, chorea or tonsillitis. He was fairly abstemious in his habits with the possible exception of a cigarette consumption of 15 daily. He had previously been an executive in a large industrial concern, but of late years had led a life of comparative ease. A recent death in the family

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had taken its toll of worry and unhappiness, but at the time of our examination his equilibrium had returned.

Examination.—The patient was an alert individual of sthenic habitus, 5 feet 6 inches tall and weighing 199 pounds. There was no objective evidence of circulatory embarrassment. The radial pulses were synchronous at 76 per minute, the accessible arteries soft, and the blood pressure was 128/74 mm. The apex beat was not palpable. No thrills were felt. Percussion elicited a normal cardiac configuration, but the left border was 1.0 cm. lateral to the midclavicular line in the fifth interspace. The heart sounds were distant and the quality was good except for slight roughening of the first sound at the apex. By fluoroscopy the lungs were normal and the diaphragm was situated rather high in the thorax. The cardiac pulsations were moderately vigorous, the aorta was not widened or elongated, and the retrocardiac space was clear. By orthodiagraphic measurement the right heart border was 5.0 cm. from the midline and the left 11.0 cm., giving a transverse cardiac diameter of 16.0 cm. which was greater than his calculated normal transverse diameter of 14.2 cm. (Eyster's method).

Laboratory Examination.—There were no abnormalities of the microscopic and chemical examinations of the blood and urine. The blood Wassermann reaction was negative by the Kahn and Kolmer technics.

ANALYSIS OF ELECTROCARDIOGRAMS

During the examination of this patient a slight transitory pulse irregularity was noted. An electrocardiogram was immediately taken in the usual manner (Fig. 1). The tracing showed a regular auricular rhythm of 75 per minute. The greater number of the ventricular complexes satisfied the criteria for the diagnosis of right bundle-branch block (old terminology), namely, the form of left axis deviation, and slurring, notching, and widening over 0.1 of the QRS groups in all leads with T directed oppositely to the major deflection. In Lead I the third ventricular beat was dropped and the ventricular complex following the fourth P-wave at an interval of 0.2 showed a pronounced change in configuration. The slurring and notching of QRS had disappeared and the QRS interval had narrowed to 0.08. The next two beats showed a return of bundle-branch block configuration after which 2:1 A-V block with constant P-R interval of 0.2 was established, halving the ventricular rate to 37.5 per minute. For the duration of this block, a period of several minutes, the intraventricular conduction disturbance did not recur. With its spontaneous disappearance and return of the ventricular rate to 75 per minute bundle-branch block reappeared (Lead II). In Lead III a dropped beat was recorded followed by one ventricular complex having a normal intraventricular conduction time. Three months later another tracing was obtained. No spontaneous changes in either A-V or intraventricular conduction were recorded. All the ventricular complexes had the bundle-branch block configuration. However, in response to pressure over the vagi in the neck, an abrupt transition to normal intraventricular conduction occurred (Fig. 2). The heart rate before this maneuver was 78.7 beats per minute. As the result of vagal pressure, the rate slowed to 56.6 per minute at which time

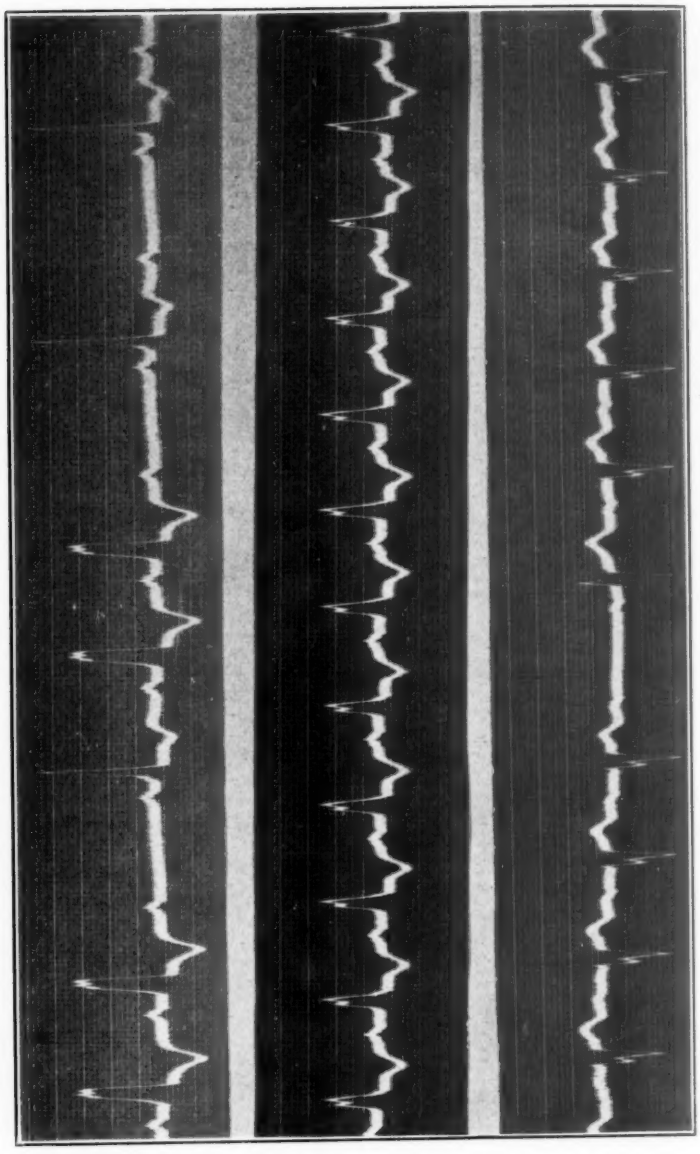

Fig. 1.—Leads I, II and III from above downward. Spontaneously occurring dropped beats and 2:1 A-V block with disappearance of the intraventricular conduction delay.

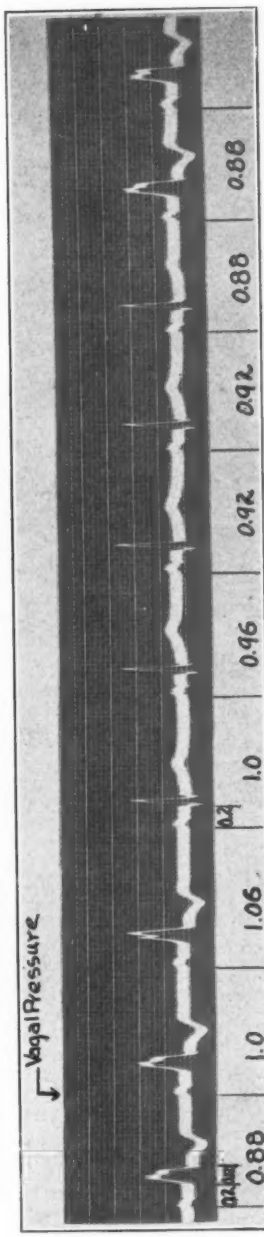

Fig. 2.—Lead II only. Cardiac slowing due to vagal pressure with abrupt cessation and return of the bundle-branch block. The vertical lines beneath the tracing represent the time in seconds between P-waves. The first transition occurs at the moment of maximum slowing; the second, when the original rate is resumed. P-R interval remains constant at 0.2.

the bundle-branch block disappeared. During five such beats the rate gradually increased to its previous level at which point the bundle-branch block was abruptly reestablished. The P-R interval remained constant at 0.2 throughout.

It should be noted that exercise had no effect upon the intr ventricular conduction time.

DISCUSSION

The classification of bundle-branch block as to type is of much theoretical interest. The reader is referred to the paper of Herrmann and Ashman for an excellent discussion of the nature of partial bundle-branch block and of the diagnostic criteria for its identification as to type.

In this instance the classification of the block could not be made from the first tracing alone. The fact that the A-V block was manifestly of type 2, shown by the dropped beats and establishment of 2:1 rhythm without prolongation of the P-R interval, gave no information as to the exact type of conduction disturbance present in the bundle. In the second tracing, however, there was recorded, as in the first three cases of Herrmann and Ashman, an abrupt transition within the space of a single cardiac cycle from bundle-branch block to normal intraventricular conduction. This makes it clear that the bundle-branch block was definitely of type 2 and as such is the fourth instance of its kind to be reported.

The fact that the transition in this instance occurred only with cardiac slowing would seem to indicate that the bundle-branch block was primarily the result of fatigue of the conduction system and that the depressed tissue was probably of very small extent. Such a conception is borne out by the fact that the patient had neither cardiac symptoms nor a clinically diagnosable heart lesion beyond a moderate hypertrophy. There seems furthermore to have occurred in this patient an improvement in the physiological state of the conduction system over a period of three months as evidenced by the disappearance of the spontaneously occurring 2:1 A-V block. It does not seem unreasonable to hope that in time the intraventricular conduction disturbance may likewise disappear. We shall watch the future course of this patient with great interest.

SUMMARY

The electrocardiographic tracings taken from a sixty-six-year-old man who had no cardiac symptoms showed a typical bundle-branch block which abruptly disappeared with the spontaneous occurrence of 2:1 A-V block, and which disappeared after cardiac slowing, the result of indirect vagal stimulation.

This is the fourth instance of proved type 2 bundle-branch block to be reported.

It is believed that the conduction disturbance in this instance was primarily the result of fatigue of the bundle and that the depressed tissue was small in extent.

REFERENCES

1. Herrmann, G., and Ashman, R.: Partial Bundle-Branch Block: A Theoretical Consideration of Transient Normal Intraventricular Conduction in the Presence of Apparently Complete Bundle-Branch Block, AM. HEART J. **6**: 375, 1931.
2. Wenckebach, K. F., and Winterberg, H.: Die Unregelmässige Herztätigkeit, Leipzig Cl, 1927, Wilhelm Engelmann.

Department of Reviews and Abstracts

Selected Abstracts

Hamilton, W. F., Spradlin, M. C., and Saam, H. G.: An Inquiry Into the Basis of the Acetylene Method of Determining the Cardiac Output. Am. J. Physiol. **100**: 587, 1932.

An attempt is made to evaluate the acetylene method of determining the cardiac output. The authors believe that while there seems to be an agreement between the acetylene method and the Fick procedure in determining the cardiac output that the acetylene method produces readings which are too low and that the source of error lies in the difficulty in determining the samples of air before the acetylene gas returns to the rebreathing chamber.

Kouwenhoven, William B., Hooker, Donald R., and Langworthy, Orthello R.: The Current Flowing Through the Heart Under Conditions of Electric Shock. Am. J. Physiol. **100**: 344, 1932.

The purpose of the experiments described in this paper was to ascertain the proportionate value of total electric current which actually flows through the heart when contact at various points on the body is made with the circuit and to determine the minimum current necessary to establish ventricular fibrillation. Dogs completely anesthetized with morphine and ether were used as experimental animals because the ventricles of the dog's heart are readily thrown into a permanent state of fibrillation by the application of relatively weak currents as is assumed to be the case in man.

It was found that 9 or 10 per cent of the total current passing through the body flows through the heart for a current pathway parallel to the body axis. When the current flows transversely, only about 3 per cent passes through the heart. Thus, as far as the heart is concerned, fibrillation will be produced by a much smaller total current flowing from the upper to the lower extremities than between the forelegs.

In most industrial accidents the current path is from the right hand to the feet and under these conditions the heart carries a greater proportion of the total current than when contact with the circuit is made at any other location on the body.

Jones, Noble W., and Newsom, S. J.: Experimentally Produced Focal (Dental) Infection in Relation to Cardiac Structure. Arch. Path. **13**: 392, 1932.

In this paper the authors present the results of their study of the following problems: (1) the relationship between experimentally produced focal (dental) infection and cardiac hypertrophy in dogs; (2) the relative effects of exercise on the hearts of such infected and noninfected dogs; (3) the reliability of the various means of expressing cardiac hypertrophy; and (4) other pathological changes cardiac and extracardiac found in the experimental animals. Dental abscesses were produced by introducing streptococcus material through an opening in the root canal of the dogs. These dental abscesses could be demonstrated in all inoculated dogs. The hearts showed constantly very small vegetative or verrucose

mitral and/or aortic endocarditic lesions, patchy parenchymatous degeneration, nuclear changes, increase in the diameter of the muscle cells and a slight round cell infiltration.

Positive relationship between experimentally produced focal dental infections and cardiac hypertrophy as measured by diameter of muscle cells was noted. Direct measurement of diameters of cardiac muscle fibers under the experimental conditions was a more reliable criterion of cardiac hypertrophy than ratios of heart weight to body weight or of heart weight to body surface area.

Stress and strain in the absence of focal infection did not affect the gross or the microscopic characteristics of the heart.

Schultz, M. P., and Swift, Homer F.: Reaction of Rabbits to Streptococci: Comparative Sensitizing Effect of Intracutaneous and Intravenous Inocula in Minute Doses. J. Exper. Med. **55**: 591, 1932.

Rabbits were rendered very hypersensitive by relatively small doses of green streptococci given intracutaneously and somewhat less hypersensitive by similar doses of heat killed vaccine prepared from hemolytic streptococci. Animals receiving the same doses intravenously gave upon subsequent testing lesions slightly more marked than normal controls, but these lesions were qualitatively hard and nodular compared with the large edematous lesions in the cutaneously sensitized group.

There was no parallelism between the degree of cutaneous or ophthalmic hypersensitivity and agglutinin titer in the blood serum. It is believed that bacterial hypersensitivity to whole streptococci appears to depend more upon previously induced focal infection than upon circulating antibodies.

McEwen, Currier: Cytologic Studies on Rheumatic Fever. 1. The Characteristic Cell of the Rheumatic Granuloma. J. Exper. Med. **55**: 745, 1932.

Scrapings of subcutaneous nodules from 10 patients with rheumatic fever were examined microscopically after being stained with supravital dyes. From the uniform results obtained the following conclusions have been drawn: (1) Supravital staining of cells from these lesions gives information unobtainable with ordinary histologic methods. (2) The scrapings show a great predominance of certain cells almost entirely devoid of phagocytic power. All the supravitally stained preparations showed small masses of tissue composed of many cells lying in a fibrillar mesh work and of wavy fibrils such as occur in similar preparations of tendons or deep fascia. Only at the margins of these masses, however, could the cells be clearly distinguished. Lying between the bits of tissue were large numbers of these same cells which because of their isolated positions could be more accurately studied. All transitions in the type of the cells were seen, ranging from small cells about the size of intermediate lymphocytes to spindle-shaped cells and large, multinucleated giant forms. The predominating cell was from 15 to 20 microns wide by 20 to 30 microns long. The small cells, however, were sometimes only 8 x 15 microns in diameter, while the multinucleated cells measured 32 x 77 microns. The shape was usually oval, but many of the cells had pointed processes at one end which were often at a sharp angle to the rest of the cell.

The cell membrane in freshly studied preparations was very indistinct but more definite in those kept in the icebox for forty-eight hours. The cytoplasma had a coarse, ground glass appearance, and its pale yellowish gray color showed it to be slightly basophilic. The nucleus was oval and large, almost filling the small cells but occupying relatively less of the larger ones. In sharp contrast to the vague cell outline, the nuclear membrane was extremely distinct. The

nuclear background had almost the same appearance as the cytoplasm, but the ground glass markings were coarser and the basophilia slightly greater. The nucleus and cytoplasm were so similar that if it had not been for the sharply outlined nuclear membrane it would have been difficult to distinguish between them. One or two nucleoli were usually present. Definite mitochondria were never seen although in a few cells a faint suggestion of minute, pale blue dots was noted. A striking contrast to this was observed in the case of lymphocytes present in small numbers in many of the preparations.

The failure of the cells to take up neutral red was their most striking characteristic which distinguishes them from monocytes, epithelioid cells and elasmatocytes; hence they differ from the essential cells of tuberculosis and experimental syphilis. These differences are probably of a functional and developmental rather than of a genetic nature. (3) The cells probably arise from the undifferentiated mesenchymal elements of loose connective tissue, although it is possible that endothelial cells take part in their formation in some instances. (4) Since there is little doubt that the subcutaneous rheumatic nodules are pathologically identical with rheumatic granulomata elsewhere in the body, these conclusions are considered applicable also to the Aschoff body cells of the myocardial submiliary nodules.

Hamilton, Joseph E., Lichty, Joseph S., and Pitts, William R.: Cardiovascular Response of Healthy Young Men to Postural Variations at Varied Temperatures. Am. J. Physiol. **100**: 383, 1932.

Tilting subjects from a horizontal to a vertical position head up, has certain effects upon the cardiovascular response at all temperatures. The systolic pressure curve remains nearly level, while the diastolic pressure steadily approaches it as the vertical position is neared. The resulting pulse pressure shows a physiological narrowing. The pulse rate rises steadily to a maximum at 80 or 90 degrees. When the subjects are returned to the horizontal position, the pulse pressure immediately widens in excess of the reading at the commencement of the experiment. The pulse rate rapidly drops.

The effects of high temperature are as follows: The systolic pressure tends to fall slightly at the higher temperatures, but since the diastolic pressure curve is lowered more than is the systolic pressure curve, the pulse pressure is wider than at room temperature. The pulse rate increases directly as the temperature. In this study there were three instances of fainting at 120° F. and one instance at 130° F. all occurring above the angles of 50°.

Tilting experiments were carried out in which the subject's ventilation was measured by means of a special spirometer. The results show a steady increase in ventilation as the subject is tilted from horizontal to vertical, a mechanism which by its aspirating effects helps to return the blood to the right heart in erect positions.

In regard to a scoring system of cardiovascular efficiency, the authors feel that the data obtained in these experiments justify only a general estimate of any given response such as "good," "fair," or "poor."

Turley, F. C., and Harrison, T. R.: Respiratory Measurements as Affected by Smoking and by Athletics. Am. J. M. Sc. **183**: 702, 1932.

Respiratory measurements were made on a group of 75 medical students and on 13 football players in active training with the idea of determining whether persons who smoke excessively are more short winded than individuals who do not smoke. As a result of these measurements of ventilation, the following conclusions may be drawn. "Heavy smoking," twenty cigarettes or more a day

for several years, does not significantly diminish the respiratory efficiency in the performance of mild and moderately severe exercise. Athletic individuals are not much more efficient than sedentary persons in the performance of mild exertion but are considerably more efficient in carrying out moderately severe exercise. Individuals who have once been highly trained remain extremely efficient in their breathing for a number of years after giving up active training provided they take fairly regular exercise.

Weiss, Soma, Robb, George P., and Ellis, Laurence B.: The Systemic Effects of of Histamine in Man With Special Reference to the Responses of the Cardiovascular System. Arch. Int. Med. **49**: 360, 1932.

A study of the systemic effects of histamine in man and a discussion of the physiological and pathological rôle of histamine based on these observations are presented.

Following the single or continuous intravenous administration of histamine, the latter is converted promptly into ineffective substances in the human body. The persistence of the action of histamine in man is of but a few minutes' duration. With uniform intravenous infusion, the bodily changes induced are practically stationary. The minimal effective amount of histamine base in man is is about 0.003 mg. per minute corresponding to a concentration of about 1:2,000,000,000 parts in the circulating blood. The maximal amount of histamine base, administered intravenously, that produces toxic manifestations is 0.15 mg. per minute.

Relatively small amounts of histamine cause a depression of the T-waves of the complexes of the normal electrocardiogram. With elevation of the dosage, the degree of depression increases until the T-wave may become inverted. After a single intravenous dose, the change in the shape of the T-wave is instantaneous with the arrival of histamine in the coronary circulation, and within one minute there is a tendency to return to the normal shape. Changes in the T-waves are not associated with any symptoms or signs referable to the heart. Histamine in amounts up to toxic doses in observations of two hours' duration fails as a rule to produce any lowering of the systolic arterial blood pressure. The diastolic arterial blood pressure shows a tendency to fall, but in numerous instances it also remains unaltered. With increasing amounts there is a progressive rise in the cardiac rate. The venous pressure is either unaltered or slightly elevated.

The effect of histamine on the cutaneous blood vessels is not uniform. The most characteristic effect is a dilatation of the venules and small veins. This effect is frequently independent of the dilator effect on the arterioles. In one group of subjects, even toxic doses fail to produce a dilatation of the arterioles as judged by the cyanotic flush and lack of elevation of the surface temperature of the skin. In a second group of subjects the arteriolar dilatation develops when a larger dose rather than one that produces a dilatation of the venules is administered. In a third group the dilatation of the arterioles and venules occurs simultaneously.

As judged from the degree of elevation of the pressure in the minute vessels of the skin, the arteriolar dilatation following large intravenous doses of histamine is slight as compared with that following the local intracutaneous application of histamine base in a solution of 1:3,000. The different types of observations presented offer conclusive evidence that the minute cerebral vessels of man respond to histamine with conspicuous dilatation. A certain parallelism exists between the sensitivity of the facial and the cerebral vessels to histamine. In a number of instances the cerebral vessels were even more sensitive than the

facial vessels, and cerebral arteriolar dilatation followed the intravenous administration of such small amounts as 0.003 mg. of histamine base.

The cardiac output per minute following the intravenous infusion of from 0.02 to 0.03 mg. of histamine base per minute increases by an average of 1.5 liters or to 20 per cent above the normal value. Simultaneously there is a slight fall in the stroke volume. The mean velocity of blood flow shows a slight but distinct increase. The basal metabolism becomes elevated and may reach values 50 per cent above the normal. There is a slight fall in the respiratory quotient.

A study of the chemical constituents and certain physical characteristics of the blood together with its hemoglobin combining power indicates that with the administration of histamine, transudation of small amounts of whole plasma occurs. This amount is too small to be demonstrated by the measurements of the total blood volume with the dye method. Histamine produces no demonstrable changes in the pulmonary ventilation or in the state of the bronchioles of normal persons, but has a definite bronchial constrictor effect on patients with bronchitis, bronchial asthma, emphysema and cardiac asthma.

Histamine when administered orally in massive doses is ineffective; hence its rôle in intestinal intoxication is highly questionable.

Evidence is presented that during the administration of histamine substances are formed or vasomotor reflexes develop which act antagonistically to histamine. The degree of peripheral vascular dilatation in man induced by histamine is not marked, and the distribution is not widespread. The vasodilator effect of histamine is promptly counteracted by an increase in the cardiac output and in other regulatory functions. A certain parallelism exists between the circulatory responses that follow exercise and those that follow the injection of histamine but this parallelism is incomplete. The vascular and other bodily responses induced by histamine in man differ fundamentally from those observed in anesthetized cats and in patients with traumatic shock. The rôle of histamine in traumatic shock is therefore considered doubtful.

Shelburne, Samuel A., Blain, Daniel, and O'Hare, James P.: The Spinal Fluid in Hypertension. J. Clin. Investigation **11**: 489, 1932.

A study of 50 cases of hypertensive disease showed 21 to have increased intracranial pressure. Papilledema and increased intracranial pressure occur more frequently with renal failure but are also found where renal function is normal. Papilledema was almost always associated with increased intracranial pressure.

Headache is more frequent in the presence of increased intracranial pressure and papilledema but occurs without either one. The results indicate that lumbar drainage for relief of headache is not justified. Increased intracranial pressure seems more often associated with high diastolic blood pressure, but the authors feel that both are probably the result of some common factor and neither is caused by the other. The cause of increased intracranial pressure is not accounted for in 50 per cent of our cases which have neither renal insufficiency nor increased venous pressure.

Heyl, Arthur F.: Auricular Paroxysmal Tachycardia Caused by Digitalis. Ann. Int. Med. **5**: 858, 1932.

The author reports the case of an adult male past middle age with hypertension and congestive heart failure in whom it was observed that digitalis which gave him relief from dyspnea, cough, edema and passive congestion at the same time induced auricular paroxysmal tachycardia followed by a two to one block in which the abnormal auricular mechanism prevailed. These abnormal rates

and rhythms occurred only as the result of digitalis administration. No other toxic symptoms due to digitalis ever occurred even with full calculated doses.

Various methods, such as effort, deeply held inspirations, forced coughing and amyl nitrite inhalations, were utilized in an attempt to induce the attacks both in the presence and in the absence of digitalis administration. When no digitalis was being administered they were consistently unsuccessful.

Various attempts were made to ascertain the effects of vagus stimulation. While he was free from digitalis, external vagus stimulation did not produce any change in the cardiac rate or rhythm nor any electrocardiographic variations. Neither did digitalis alone even in full dosage slow the rate as would have been true had it acted directly on the vagus.

The author points out that graphic methods are especially favorable for diagnosis in patients with sinus tachycardia, particularly in those who need and are receiving digitalis. In this instance even mild doses repeatedly resulted in auricular paroxysmal tachycardia with or without a two to one block with a rapid ventricular rate which without electrocardiographic control might naturally have led to the futile use of more digitalis and increased toxicity in an effort either to slow the ventricular rate or to prevent the often recurring "clinical" auricular paroxysmal tachycardia.

Duff, G. Lyman: Medial Degeneration in the Aorta of the Rabbit Produced by Diphtheria Toxin. Arch. Path. **13**: 543, 1932.

Successive intravenous injections of diphtheria toxin in suitable quantities produce in rabbits severe medial degeneration of the aorta and its large branches within from eight to fourteen days. Damage to the arteries is probably the result of the direct toxic action of diphtheria toxin on the media.

The changes in the media are most marked in the arch and thoracic portion of the aorta resulting in thinning of the arterial wall, dilatation and the formation of aneurysmal sacs. With the establishment of calcification, transverse fissures appear on the intimal surface. The lesion commences in the middle third of the media primarily as a cloudy swelling, degeneration and necrosis of muscle fibers. Fatty changes occur in the process at least in its later stages. Elastic fibers, slightly later, also undergo degeneration with the loss of elasticity and the development of stiffness and rigidity even before the appearance of calcification. Calcification is first seen as a finely granular deposit in the debris of degenerated muscle fibers but later involves also the elastic fibers and becomes most prominent in them. These changes were found in young animals and are different from those which are observed in older animals.

Direct application of these results to human diphtheria is rather precarious. One might suggest, however, the possibility of a relationship. Many investigators have questioned the statement that damage to the heart alone is sufficient to account for the circulatory collapse in rapidly fatal cases of diphtheria. Accordingly, damage to vasomotor centers has been invoked as a factor contributing to this collapse. It would seem at least possible from the present experiments that direct damage to peripheral arteries may also have a bearing on this phenomenon.

Alstead, Stanley: The Electrocardiogram in Diphtheria. Quart. J. Med. **1**: 277, 1932.

The object of this investigation was to attempt to define the changes commonly seen in the electrocardiogram in the course of diphtheria, to correlate them to the clinical condition and to assess the value of this form of investigation in a fever hospital.

It was found that while a large proportion of cases having mild myocarditis are undetected by clinical methods, such cases become comparatively rare in the moderate and severe types of diphtheria. Hence for practical purposes the character of the heart sounds is usually a sufficiently accurate guide to the state of the myocardium.

Of the various physical signs in the heart taken to indicate myocarditis in diphtheria, the most valuable as confirmed by simultaneous electrocardiographic records are: (a) progressive softening of the first heart sound at all areas especially the mitral and aortic areas; (b) the character of the cardiac impulse at the apex and movement of the apex beat to a position farther away from the midline; (c) splitting of the first mitral sound producing a triple rhythm.

Serial electrocardiographic records show that with the onset of diphtheritic paralyses there is in a considerable proportion of cases a simultaneous relapse in the condition of the heart. This fact is much less frequently observed when clinical methods alone are employed. Although gross degeneration of the heart muscle and specialized conducting system are frequently shown by the electrocardiograph during diphtheria these lesions are mostly transient. Complete heart block is by far the commonest lesion associated with circulatory collapse ending fatally, but complete block is probably only a contributory factor in a condition characterized by widespread changes in the circulatory system.

The severity of the cardiac lesion is usually proportional to the severity of the toxemia when specific treatment is commenced. There are, however, cases in which neither the clinical nor the electrocardiographic abnormalities are sufficient to account for the state of impending circulatory collapse which is often seen in diphtheria.

It is concluded that the electrocardiograph is a valuable means of estimating the severity of diphtheritic myocarditis and the only means of accurate diagnosis of conductive lesions in the majority of cases. The clinical signs which are most closely related to the electrocardiographic findings are those dependent on cardiac function. The significance of persistently abnormal heart sounds can be safely estimated by the electrocardiogram and the patient's response to effort considered together.

Salley, S. M.: An Unusual Atropin Effect on Ventricular Tachycardia. Am. J. M. Sc. **183**: 456, 1932.

A case of coronary thrombosis was observed showing ventricular tachycardia with a rapid ventricular rate. The ventricular rate was frequently slowed by increasing doses of quinidin to 110 or 115, but the tachycardia could not be abolished. Immediately following one dose of 0.002 gm. of atropin sulphate this abnormal mechanism disappeared uncovering complete heart block with a slow idioventricular rhythm. It is believed that the circus movement was broken up by atropin through its paralyzing effect on the vagus.

Nathanson, M. H.: Coronary Disease in 100 Autopsied Diabetics. Am. J. M. Sc. **183**: 495, 1932.

An analysis of 100 autopsies upon diabetics shows an incidence of 41 per cent of severe coronary disease. Above the age of fifty years the incidence is 52.7 per cent as compared with 8 per cent in an even larger series of nondiabetics of the same age. The frequency of coronary disease is almost as high in the female as the male.

The incidence of hypertensive hypertrophy of the heart indicates that hypertension is only slightly more frequent in the diabetics than the nondiabetics. In diabetics with gangrene the incidence of coronary disease is higher than

in the uncomplicated cases. The essential cardiac lesion of diabetes is coronary sclerosis. Other types of cardiac disease are of relatively rare occurrence. The etiological relationship between diabetes and arteriosclerosis is discussed.

Brown, Herbert H.: Tooth Extraction and Chronic Infective Endocarditis. Brit. M. J. **1**: 796, 1932.

The danger of extracting teeth with apical streptococcal infection is a real one, and the author feels convinced that the danger is increased if local anesthesia by infiltration of the gum is made use of. It is not feasible to estimate beforehand the patient's resistance to the infecting organism and cultures often cannot be made until the tooth is extracted.

It is suggested that as a precaution, especially in the case of an individual already suffering from valvular disease or one who may seem for other reasons to be liable to have a weak resistance, to extract one tooth only in the first instance under a general anesthesia. Under these conditions, a culture may be made and, if possible, the patient's blood may be tested for bactericidal power against the organism.

Brown, George E.: Erythromelalgia and Other Disturbances of the Extremities Accompanied by Vasodilatation and Burning. Am. J. M. Sc. **183**: 468, 1932.

A series of 81 patients whose major complaint was burning in the feet or hands was studied to determine the relationship, if any, of the burning distress to the surface temperature of the affected part, the variation in surface temperature and local symptoms in relation to posture, exercise and exposure to heat and cold: to determine in a small group of patients by the method of inducing fever, by injection of foreign proteins, the thresholds for perception of the burning sensation, in relation to surface temperature regions in which the burning was felt, and whether or not the patients could be relieved in cases in which the burning distress of a paresthetic type was present by inducing spinal anesthesia to the point of total analgesia in the feet.

The author discusses the difficulties in establishing a diagnosis of this disease. Four fundamental criteria which are essential are mentioned. The methods of study to distinguish between the different conditions in which burning extremities occur are outlined. The treatment of this condition remains unsatisfactory.

Pearse, Herman E., and Morton, John J.: The Blood Pressure in the Arteries of the Extremities in Normal Subjects and in Patients With Peripheral Vascular Disease. Am. J. M. Sc. **183**: 485, 1932.

The effect of altering the position of a limb on the blood pressure of the peripheral arteries has been studied. It was found that alteration of an extremity lowered the blood pressure while its depression raised the intraventricular pressure. These results correlated with the theoretical hydrostatic change of such a maneuver.

In peripheral vascular lesions it is essential to know the condition of the main arteries as well as that of the arteriolar and subpapillary branches. The vasoconstrictor influence upon the latter structures is demonstrated by a skin temperature response to known agents. The state of the main vessels can only be determined by estimation of the perceptible pulse or by oscillometry.

In the past the Pachon instrument has been the standard for oscillometric determinations. The Tycos recording sphygmomanometer has the advantage of giving an accurate, permanent calibrated record for this purpose. The use of this instrument with the special cuffs devised is considered desirable not only to determine the condition of the vessels in disease but also to study vascular physiology.

Book Reviews

DISEASES OF THE CORONARY ARTERIES (Myocarditis). By Don C. Sutton and Harold Lueth. The C. V. Mosby Company, Saint Louis, 1932, pp. 164.

This volume is evidence of the increasing interest in arteriosclerotic heart disease (one regrets that the authors retain the term "Chronic myocarditis"), and while it does not add new facts to our knowledge it brings together, especially for the clinician, many recent observations. The book is generously illustrated and contains many references, quotations, and case reports; it gives evidence, however, of hasty preparation. The interpretation of several of the electrocardiograms is open to serious question and some of the quotations fail to illustrate the subject under discussion. The book is evidently the result of independent investigation and wide reading, and the bibliography alone would repay careful study. *E. H.*

SEMIOLOGIA DE LA ONDA T DEL ELECTROCARDIOGRAMA Y SU INTREPRETACION CLINICA. By Antonio Battro. Buenos Aires, 1931, Sebastian de Amorrortu.

This monograph of 120 pages with 66 illustrations is concerned solely with the T-wave of the electrocardiogram, its form and significance in tracings from persons with normal hearts and in those from patients with various types of heart disease. There is also a discussion of the prognostic value of changes in the T-wave. It is a careful and detailed study of a limited field. *E. H.*

KLINISCHE ELEKTROKARDIOGRAPHIE MIT EINEM GRUNDRISS DER ARHYTHMIEN. By Dr. Wilhelm Dressler, assistant at the Herzstation in Vienna. With an introduction by Prof. Dr. C. J. Rothberger. Second, revised edition, with 118 illustrations. Berlin and Vienna, 1932, Urban & Schwarzenberg.

This volume was written to supply the need in the German clinics for a clinical book on electrocardiography.

The introduction by Professor Rothberger emphasizes the importance of this need, and the fact that such books have appeared in English and American literature for many years and have been of great educational value to the general practitioner.

The book follows very closely the general scheme of similar books published by American authors. It fulfills its purpose in that it gives the general practitioner an excellent idea of what the electrocardiogram is, and what information it may convey.

The section on the electrocardiographic evidences of myocardial disease is unusually good. Unfortunately the author at times gives only single leads to illustrate the cardiac disturbances. The time marker also is missing from many of the curves, and in others it is very indistinct.

Dr. Dressler still adheres to the original description of right and left bundle-branch block. The recent interpretation of bundle-branch block will doubtless be incorporated in the next edition.

The clinical manifestations of the various cardiac disturbances are given in rather sketchy fashion and there is no bibliography.

M. A. R.